Search Results - Record(s) 1 through 11 of 11 returned.

1. Document ID: US 5849992 A
Entry 1 of 11 File: USPT Dec 15, 1998

US-PAT-NO: 5849992
DOCUMENT-IDENTIFIER: US 5849992 A
TITLE: Transgenic production of antibodies in milk

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

2. Document ID: US 5843705 A
Entry 2 of 11 File: USPT Dec 1, 1998

US-PAT-NO: 5843705
DOCUMENT-IDENTIFIER: US 5843705 A
TITLE: Transgenically produced antithrombin III

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

3. Document ID: US 5827690 A
Entry 3 of 11 File: USPT Oct 27, 1998

US-PAT-NO: 5827690
DOCUMENT-IDENTIFIER: US 5827690 A
TITLE: Transgenic production of antibodies in milk

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

4. Document ID: US 5750172 A
Entry 4 of 11 File: USPT May 12, 1998

US-PAT-NO: 5750172
DOCUMENT-IDENTIFIER: US 5750172 A
TITLE: Transgenic non human mammal milk

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

5. Document ID: US 4873316 A
Entry 5 of 11 File: USPT Oct 10, 1989

US-PAT-NO: 4873316
DOCUMENT-IDENTIFIER: US 4873316 A
TITLE: Isolation of exogenous recombinant proteins from the milk of transgenic mammals

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

6. Document ID: US 5750172 A
Entry 6 of 11

File: EPAB

May 12, 19

PUB-NO: US005750172A
DOCUMENT-IDENTIFIER: US 5750172 A
TITLE: Transgenic non human mammal milk

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

7. Document ID: WO 9837224 A1
Entry 7 of 11

File: EPAB

Aug 27, 1998

PUB-NO: WO009837224A1
DOCUMENT-IDENTIFIER: WO 9837224 A1
TITLE: TRANSGENICALLY PRODUCED NON-SECRETED PROTEINS

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

8. Document ID: WO 9626268 A1
Entry 8 of 11

File: EPAB

Aug 29, 1996

PUB-NO: WO009626268A1
DOCUMENT-IDENTIFIER: WO 9626268 A1
TITLE: TRANSGENICALLY PRODUCED ANTITHROMBIN III

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

9. Document ID: WO 9517085 A1
Entry 9 of 11

File: EPAB

Jun 29, 1995

PUB-NO: WO009517085A1
DOCUMENT-IDENTIFIER: WO 9517085 A1
TITLE: TRANSGENIC PRODUCTION OF ANTIBODIES IN MILK

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

10. Document ID: WO 9113151 A1
Entry 10 of 11

File: EPAB

Sep 5, 1991

PUB-NO: WO009113151A1
DOCUMENT-IDENTIFIER: WO 9113151 A1
TITLE: IMPROVED EXPRESSION OF POLYPEPTIDES

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Clip Img | Image

11. Document ID: US 4873316 A
Entry 11 of 11

File: EPAB

Oct 10, 1989

PUB-NO: US004873316A
DOCUMENT-IDENTIFIER: US 4873316 A
TITLE: Isolation of exogenous recombinant proteins from the milk of transgenic mammals

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

Terms	Documents
meade-harry.in.	11

********** STN Columbus **********

FILE 'HOME' ENTERED AT 16:55:03 ON 04 AUG 1999

=> file medline

COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.15 0.15

FILE 'MEDLINE' ENTERED AT 16:55:09 ON 04 AUG 1999

FILE LAST UPDATED: 30 JUL 1999 (19990730/UP). FILE COVERS 1960 TO DATE.

MEDLINE has been reloaded to reflect the annual MeSH changes made by
the National Library of Medicine for 1999. Enter HELP RLOAD for details.

OLDMEDLINE, data from 1960 through 1965 from the Cumulated Index
Medicus (CIM), has been added to MEDLINE. See HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the
Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
SUBSTANCE IDENTIFICATION.

=> s immunoglobulin and whey acidic protein/ab,bi

'AB' IS NOT A VALID FIELD CODE
66111 IMMUNOGLOBULIN
0 WHEY ACIDIC PROTEIN/AB
1812 WHEY/BI
32864 ACIDIC/BI
829012 PROTEIN/BI
145 WHEY ACIDIC PROTEIN/BI
((WHEY(W)ACIDIC(W)PROTEIN)/BI)
L1 4 IMMUNOGLOBULIN AND WHEY ACIDIC PROTEIN/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L1 ANSWER 1 OF 4 MEDLINE
AN 1998455664 MEDLINE
DN 98455664
TI Lactogenic immunity in transgenic mice producing recombinant antibodies
neutralizing coronavirus.
AU Castilla J; Sola I; Pintado B; Sanchez-Morgado J M; Enjuanes L
CS Department of Molecular and Cell Biology, Centro Nacional de Biotecnologia, CSIC, Madrid, Spain.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 440 675-86.
Journal code: 2LU. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
EW 19990303
AB Protection against coronavirus infections can be provided by the oral
administration of virus neutralizing antibodies. To provide lactogenic
immunity, eighteen lines of transgenic mice secreting a recombinant IgG1
monoclonal antibody (rIgG1) and ten lines of transgenic mice secreting
recombinant IgA monoclonal antibodies (rIgA) neutralizing transmissible
gastroenteritis coronavirus (TGEV) into the milk were generated. Genes
encoding the light and heavy chains of monoclonal antibody (MAb) 6A.C3
were expressed under the control of regulatory sequences derived from the
mouse genomic DNA encoding the ***whey*** ***acidic*** ***protein*** (WAP) and beta-lactoglobulin (BLG), which are highly
abundant milk proteins. The MAb 6A.C3 binds to a highly conserved epitope
present in coronaviruses of several species. This MAb does not allow the
selection of neutralization escaping virus mutants. The antibody was
expressed in the milk of transgenic mice with titers of one million as
determined by RIA, and neutralized TGEV infectivity by one million fold
corresponding to ***immunoglobulin*** concentrations of 5 to 6 mg per
ml. Matrix attachment regions (MAR) sequences were not essential for rIgG1
transgene expression, but co-microinjection of MAR and antibody genes led
to a twenty to ten thousand-fold increase in the antibody titer in 50% of
the rIgG1 transgenic animals generated. Co-microinjection of the genomic
BLG gene with rIgA light and heavy chain genes led to the generation of
transgenic mice carrying the three transgenes. The highest antibody titers
were produced by transgenic mice that had integrated the antibody and BLG
genes, although the number of transgenic animals generated does not allow
a definitive conclusion on the enhancing effect of BLG co-integration.
Antibody expression levels were transgene copy number independent and
integration site dependent. The generation of transgenic animals producing
virus neutralizing antibodies in the milk could be a general approach to
provide protection against neonatal infections of the enteric tract.

L1 ANSWER 2 OF 4 MEDLINE
AN 1998040670 MEDLINE
DN 98040670
TI Production of active anti-CD6 mouse/human chimeric antibodies in the milk
of transgenic mice.
AU Limonta J; Pedraza A; Rodriguez A; Freyre F M; Barral A M; Castro F O;
Lleonart R; Gracia C A; Gavilondo J V; de la Fuente J
CS Mammalian Cell Genetics Division, Center for Genetic Engineering and
Biotechnology, Havana, Cuba.
SO IMMUNOTECHNOLOGY, (1995 Aug) 1 (2) 107-13.
Journal code: CR0. ISSN: 1380-2933.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
EW 19980302
AB The expression of chimeric genes in the mammary gland of transgenic farm
animals has become an alternative for the large-scale production of
recombinant proteins and for the modification of milk composition. In this
paper, we show that a mouse/human chimeric antibody against the human CD6
leukocyte antigen can be assembled and correctly folded by the mammary
gland, and secreted to milk, where it maintains its specificity. The base
sequences encoding for the heavy and light chain variable regions of the
anti-CD6 mouse monoclonal antibody IOR-T1 were cloned by the polymerase
chain reaction from hybridoma cDNA, coupled to human heavy and light chain
constant region genes, and inserted in a vector containing the 5'
regulatory region of the rabbit ***whey*** ***acidic*** ***protein*** gene. Transgenic mice were produced by conventional

pronuclei microinjection techniques. Integration and transgene copy number
were determined by Southern blot. Assembled human ***immunoglobulin*** was detected in milk using a sandwich ELISA. Expression levels of chimeric
antibodies in milk were determined to be around 400 micrograms/ml by
Western blot, using CHO-derived chimeric IOR-T1 antibodies as reference.
The chimeric antibodies produced in milk recognized human peripheral blood
T lymphocytes by indirect immunofluorescence, with the classical patch-like pattern of IOR-T1.

L1 ANSWER 3 OF 4 MEDLINE
AN 95358828 MEDLINE
DN 95358828
TI The effect of various introns and transcription terminators on the efficiency of expression vectors in various cultured cell lines and in the
mammary gland of transgenic mice.
AU Petitclerc D; Attal J; Theron M C; Bearzotti M; Bolifraud P; Kann G;
Stinnakre M G; Pointu H; Puissant C; Houdebine L M
CS Agriculture et Agro-Alimentaire Canada, Est Lennoxville, Quebec.
SO JOURNAL OF BIOTECHNOLOGY, (1995 Jun 21) 40 (3) 169-78.
Journal code: AL6. ISSN: 0168-1656.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; B
EM 199511
AB Various combinations of promoters, introns and transcription terminators
were used to drive the expression of bovine growth hormone (bGH) cDNA in
different cell types. In constructs containing the human cytomegalovirus
(hCMV) promoter and the SV40 late genes terminator, the intron from SV40
genes (VP1) was much more efficient, than the intron from the early genes
(t). The synthetic intron SIS generated by the association of an
adenovirus splice donor and an ***immunoglobulin*** G splice acceptor
showed the highest activity. The respective potency of these introns was
similar in several mammalian (CHO, HC11 and COS) and fish (TO2 and EPC)
cells. The rabbit ***whey*** ***acidic*** ***protein*** (WAP)
gene promoter was highly efficient to drive the expression of bGH gene in
the HC11 mammary cell lines. In contrast, the bGH cDNA under the control
of the same promoter was much less efficiently expressed when the SV40 VP1
intron and transcription terminator were used. The rabbit WAP gene and the
human GH gene terminators did not or only moderately enhanced the
expression of the construct WAP bGH cDNA. Introduction of a promoter
sequence from the mouse mammary tumor virus (MMTV) LTR in the VP1 intron
increased very significantly the expression of the WAP bGH cDNA. Although
several of these vectors showed high potency when expressed stably in HC11
cells, all of them were only moderately efficient in transgenic mice.
These data indicate that the VP1 and the SIS introns may be used to
express foreign cDNAs with good efficiency in different cell types. The
addition of an enhancer within an intron may still reinforce its
efficiency. However, transfection experiments, even when stable expression
is carried out, are poorly predictive of the potential efficiency of a
vector in transgenic animals.

L1 ANSWER 4 OF 4 MEDLINE
AN 93173503 MEDLINE
DN 93173503
TI T1, an ***immunoglobulin*** superfamily member, is expressed in
H-ras-dependent epithelial tumours of mammary cells.
AU Rossler U; Andres A C; Reichmann E; Schmahl W; Werenskiold A K
CS Department of Cell Chemistry, GSF-Forschungszentrum fur Umwelt und
Gesundheit, Neuherberg, Germany..
SO ONCOGENE, (1993 Mar) 8 (3) 609-17.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199305
AB T1 is a glycosylated protein in the carcinoembryonic antigen (CEA) family
of tumour marker molecules. It was originally identified by virtue of its
transient induction after the expression of p21H-ras in NIH3T3
fibroblasts. Here we show that the T1 gene is activated in mammary
adenocarcinomas of transgenic mice harbouring an H-ras transgene under the
control of the mammary-specific ***whey*** ***acidic***
protein (WAP) promoter. By contrast, T1 mRNA was not, or only
faintly, detectable in mammary carcinomas of transgenic mice bearing a
WAP-myc transgene. Thus, T1 overexpression does not appear to be a general
tumour-specific phenomenon. A dependence of T1 gene expression on the
action of p21H-ras is suggested by the observation of T1 mRNA in nude
mouse tumours generated from H-ras-transformed cultured mammary epithelial
cells. Interestingly, activation of the T1 gene is also found during the
maturation of the mammary gland (3-4 weeks after birth), whereas it is
absent during its terminal differentiation in pregnancy and lactation.
This expression pattern suggests a role for the secreted T1 glycoprotein
in the phase of epithelial proliferation of the mammary gland. It appears
that p21H-ras-induced transformation of mammary epithelial cells mimics
the situation occurring in puberty. In both developmental stages the T1
glycoprotein might affect cell interactions of the proliferating
epithelial cells with the surrounding stroma. It might thus promote ductal
outgrowth in gland maturation as well as invasive growth of
p21H-ras-transformed mammary epithelial cells.

=> s immunoglobulin# and whey acidic protein/ab,bi

'AB' IS NOT A VALID FIELD CODE
108494 IMMUNOGLOBULIN#
0 WHEY ACIDIC PROTEIN/AB
1812 WHEY/BI
32864 ACIDIC/BI
829012 PROTEIN/BI
145 WHEY ACIDIC PROTEIN/BI
((WHEY(W)ACIDIC(W)PROTEIN)/BI)
L2 4 IMMUNOGLOBULIN# AND WHEY ACIDIC PROTEIN/AB,BI

=> s immunoglobulin# and beta-lactoglobulin promoter/ab,bi

'AB' IS NOT A VALID FIELD CODE
108494 IMMUNOGLOBULIN#
0 BETA-LACTOGLOBULIN PROMOTER/AB
350029 BETA/BI
1402 LACTOGLOBULIN/BI
61727 PROMOTER/BI
22 BETA-LACTOGLOBULIN PROMOTER/BI
((BETA(W)LACTOGLOBULIN(W)PROMOTER)/BI)
L3 0 IMMUNOGLOBULIN# AND BETA-LACTOGLOBULIN PROMOTER/AB,BI

=> s immunoglobulin# and casein promoter/ab,bi

'AB' IS NOT A VALID FIELD CODE
108494 IMMUNOGLOBULIN#

```
        0 CASEIN PROMOTER/AB
    11523 CASEIN/BI
    61727 PROMOTER/BI
       46 CASEIN PROMOTER/BI
          ((CASEIN(W)PROMOTER)/BI)
L4      0 IMMUNOGLOBULIN# AND CASEIN
PROMOTER/AB,BI

=> s immunoglobulin# and beta-casein promoter/ab,bi

'AB' IS NOT A VALID FIELD CODE
   108494 IMMUNOGLOBULIN#
        0 BETA-CASEIN PROMOTER/AB
   350029 BETA/BI
    11523 CASEIN/BI
    61727 PROMOTER/BI
       44 BETA-CASEIN PROMOTER/BI
          ((BETA(W)CASEIN(W)PROMOTER)/BI)
L5      0 IMMUNOGLOBULIN# AND BETA-CASEIN
PROMOTER/AB,BI

=> s immunoglobulin# and kappa-casein promoter/ab,bi

'AB' IS NOT A VALID FIELD CODE
   108494 IMMUNOGLOBULIN#
        0 KAPPA-CASEIN PROMOTER/AB
    21261 KAPPA/BI
    11523 CASEIN/BI
    61727 PROMOTER/BI
        0 KAPPA-CASEIN PROMOTER/BI
          ((KAPPA(W)CASEIN(W)PROMOTER)/BI)
L6      0 IMMUNOGLOBULIN# AND KAPPA-CASEIN
PROMOTER/AB,BI

=> s immunoglobulin# and lactalbumin promoter/ab,bi

'AB' IS NOT A VALID FIELD CODE
   108494 IMMUNOGLOBULIN#
        0 LACTALBUMIN PROMOTER/AB
     2108 LACTALBUMIN/BI
    61727 PROMOTER/BI
        3 LACTALBUMIN PROMOTER/BI
          ((LACTALBUMIN(W)PROMOTER)/BI)
L7      0 IMMUNOGLOBULIN# AND LACTALBUMIN
PROMOTER/AB,BI

=> s immunoglobulin# and lactalbumin/ab,bi

'AB' IS NOT A VALID FIELD CODE
   108494 IMMUNOGLOBULIN#
        0 LACTALBUMIN/AB
     2108 LACTALBUMIN/BI
L8     96 IMMUNOGLOBULIN# AND LACTALBUMIN/AB,BI

=> s l8 and (construct# or vector#)/ab,bi

'AB' IS NOT A VALID FIELD CODE
        0 CONSTRUCT#/AB
    26298 CONSTRUCT#/BI
        0 VECTOR#/AB
    59832 VECTOR#/BI
L9      0 L8 AND (CONSTRUCT# OR VECTOR#)/AB,BI

=> s l8 and transgen?/ab,bi

'AB' IS NOT A VALID FIELD CODE
        0 TRANSGEN?/AB
    22862 TRANSGEN?/BI
L10     0 L8 AND TRANSGEN?/AB,BI

=> s immunoglobulin# and casein/ab,bi

'AB' IS NOT A VALID FIELD CODE
   108494 IMMUNOGLOBULIN#
        0 CASEIN/AB
    11523 CASEIN/BI
L11   190 IMMUNOGLOBULIN# AND CASEIN/AB,BI

=> s l11 and (construct# or vector#)/ab,bi

'AB' IS NOT A VALID FIELD CODE
        0 CONSTRUCT#/AB
    26298 CONSTRUCT#/BI
        0 VECTOR#/AB
    59832 VECTOR#/BI
L12     8 L11 AND (CONSTRUCT# OR VECTOR#)/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 8 ANSWERS -
CONTINUE? Y/(N):y


L12 ANSWER 1 OF 8 MEDLINE
AN  1999150486    MEDLINE
DN  99150486
TI  Construction of phosphorylatable chimeric monoclonal antibody
CC49 with a
      ***casein***  kinase I recognition site.
AU  Lin L; Gillies S D; Schlom J; Pestka S
CS  University of Medicine and Dentistry of New Jersey-Robert
Wood Johnson
    Medical School, 675 Hoes Lane, Piscataway, New Jersey,
08854-5635, USA.
NC  RO1 CA46465 (NCI)
    RO1 CA52363 (NCI)
SO  PROTEIN EXPRESSION AND PURIFICATION, (1999 Feb)
15 (1) 83-91.
    Journal code: BJV. ISSN: 1046-5928.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Priority Journals
EM  199905
EW  19990503
AB  Phosphorylation sites for  ***casein***  kinase I were
introduced into
    chimeric monoclonal antibody CC49 (MAb-chCC49) by inserting a
synthetic
    fragment (CK1) encoding two  ***casein***  kinase I
phosphorylation
    sites into an expression  ***vector***  . The phosphorylation sites
were
    created by incorporating the predicted consensus sequences for
    phosphorylation by the  ***casein***  kinase I at the carboxyl
terminus
    of the heavy-chain constant region of the MAb-chCC49. The
resultant
    modified MAb-chCC49 (MAb-chCC49CK1) was expressed and
purified. The
    MAb-chCC49CK1 protein can be phosphorylated by the
***casein***  kinase
    I with [gamma-32P]ATP to high radiospecific activity. The
32P-labeled
    MAb-chCC49CK1 protein binds to cells expressing TAG-72
antigens. The
    introduction of phosphorylation sites into MAb provides new
reagents for
    the diagnosis and treatment of cancer. This demonstrates that, as
was
    described for the cAMP-dependent protein kinase site, the
***casein***
    kinase I recognition site can also be used to introduce
phosphorylation
    sites into proteins. Copyright 1999 Academic Press.

L12 ANSWER 2 OF 8 MEDLINE
AN  97138303    MEDLINE
DN  97138303
TI  Varicella-zoster virus Fc receptor gE glycoprotein:
serine/threonine and
    tyrosine phosphorylation of monomeric and dimeric forms.
AU  Olson J K; Bishop G A; Grose C
CS  Department of Microbiology and Immunology Program,
University of Iowa
    College of Medicine, Iowa City 52242, USA.
NC  AI22795 (NIAID)
    AI28847 (NIAID)
SO  JOURNAL OF VIROLOGY, (1997 Jan) 71 (1) 110-9.
    Journal code: KCV. ISSN: 0022-538X.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Priority Journals; Cancer Journals
EM  199704
EW  19970402
AB  Varicella-zoster virus (VZV) glycoprotein gE is the predominant
viral cell
    surface molecule; it behaves as an Fc receptor for
***immunoglobulin***
    G, but its central function may be more closely related to viral
```

egress
and cell-to-cell spread. To further analyze the receptor properties of VZV
gE, the gE gene (also called open reading frame 68) was expressed by a
baculovirus ***vector*** in insect cells. The recombinant baculovirus
gE product had a molecular mass of 64 kDa, smaller than the previously
documented 98 kDa of mature gE expressed in mammalian cells. The major
reason for the lowered molecular mass was diminished glycosylation. In
addition to the 64-kDa form, a larger (130-kDa) form was observed in
insect cells and represented dimerized 64-kDa molecules. Both the
monomeric and dimeric gE forms were highly phosphorylated in insect cells.
Protein kinase assays conducted in vitro with [gamma-32P]ATP and
[gamma-32P]GTP indicated that endogenous ***casein*** kinase II was
phosphorylating monomeric gE, while the dimeric gE form was phosphorylated
by another kinase which did not utilize [gamma-32P]GTP. When immobilized
recombinant gE molecules were probed with a monoclonal antibody which
specifically recognizes a phosphotyrosine linkage, the gE dimer was found
to be tyrosine phosphorylated whereas the monomer was not similarly
modified. When recombinant gE produced in HeLa cells was probed with the
same antiphosphotyrosine antibody, a dimeric gE form at 130 kDa was
detected on the cell surface. These results suggested that VZV gE closely
resembled other cell surface receptors, being modified on its various
forms by both serine/threonine and tyrosine protein kinases. In this case,
tyrosine phosphorylation occurred on a previously unrecognized and
underglycosylated VZV gE dimeric product.

L12 ANSWER 3 OF 8 MEDLINE
AN 96375171 MEDLINE
DN 96375171
TI Efficient vasoactive intestinal polypeptide hydrolyzing autoantibody light
chains selected by phage display.
AU Tyutyulkova S; Gao Q S; Thompson A; Rennard S; Paul S
CS Department of Anesthesiology, University of Nebraska Medical Center,
Omaha, USA.
NC HL44126 (NHLBI)
AI31268 (NIAID)
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Aug 23) 1316 (3) 217-23.
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-L43498; GENBANK-L43499
EM 199612
AB An ***immunoglobulin*** light chain (L chain) library derived from the
peripheral blood lymphocytes of a patient with asthma was cloned into a
phagemid ***vector*** . Phage particles displaying L chains capable of
binding vasoactive intestinal polypeptide (VIP) were isolated by affinity
chromatography. Two VIP binding L chains were expressed in Escherichia
coli in soluble form and purified to electrophoretic homogeneity by metal
chelating and protein L affinity chromatography. Both L chains catalyzed
the hydrolysis of [tyr10-125I]VIP substrate. The catalytic activity eluted
at the molecular mass of the monomer form of the L chain (28 kDa) from a
gel filtration column. The activity was bound by immobilized
anti-kappa-chain antibody. A control recombinant L chain displayed no
catalytic activity. Hydrolysis of VIP by the catalytic L chains was
saturable and consistent with Michaelis-Menten kinetics. The turnover of
the L chains was moderate (0.22 and 2.21/min) and their Km values
indicated comparatively high affinity recognition of VIP[111 and 202 nM),
producing catalytic efficiencies comparable to or greater than trypsin.
Unlike trypsin, the L chains did not display detectable cleavage of
casein , suggesting a catalytic activity specialized for VIP.
Comparisons of the nucleotide sequences of the L chain cDNA with their
putative germ-line counterparts suggested the presence of several
replacement mutations in the complementarity determining regions (CDRs).
These observations suggest: (a) Retention or acquisition of catalytic
activity by the L chains is compatible with affinity maturation of
antibodies; and (b) The autoimmune L chain repertoire can serve as a
source of substrate-specific and efficient catalysts.

L12 ANSWER 4 OF 8 MEDLINE
AN 93234096 MEDLINE
DN 93234096
TI Expression of Porphyromonas gingivalis proteolytic activity in Escherichia
coli.
AU Madden T E; Thompson T M; Clark V L
CS Department of Dental Research, University of Rochester, New York..
NC 5R01 DE08512 (NIDR)
5K16 DE00159 (NIDR)
SO ORAL MICROBIOLOGY AND IMMUNOLOGY, (1992 Dec) 7 (6) 349-56.
Journal code: ORA. ISSN: 0902-0055.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Dental Journals; Dental
EM 199307
AB Porphyromonas gingivalis (formerly Bacteroides gingivalis) degrades
numerous protein substrates including collagen, fibrinogen, fibronectin,
gelatin, ***casein*** , ***immunoglobulins*** and complement
components. In order to clone one or more of these protease genes, a
genomic library was constructed with Sau3A1 restriction fragments of
chromosomal DNA from P. gingivalis ATCC 33277 ligated into the
temperature-regulated ***vector*** pCQV2, and expressed in Escherichia
coli DH5 alpha mcr. The electro-transformants (3 x 10(4)) were screened
for general protease activity on Luria broth agar containing ampicillin
(50 mg/l) and sodium caseinate (2%). One ***casein*** -hydrolyzing
clone was detected and subcultured, and the activity of the cell extracts
was characterized. We were able to show that the protease-positive clone,
(pTEM1), had broad substrate specificity. Colorimetric assays indicated
the hydrolysis of azocoll, azocasein, collagen, elastin-congo red and
artificial substrates. Sodium dodecyl sulfate-polyacrylamide gel
electrophoresis was used to confirm that collagen, ***casein*** ,
fibrinogen and fibronectin were degraded by the clone.

L12 ANSWER 5 OF 8 MEDLINE
AN 93206099 MEDLINE
DN 93206099
TI Effect of PU.1 phosphorylation on interaction with NF-EM5 and
transcriptional activation.
AU Pongubala J M; Van Beveren C; Nagulapalli S; Klemsz M J; McKercher S R;
Maki R A; Atchison M L
CS Department of Animal Biology, University of Pennsylvania, School of
Veterinary Medicine, Philadelphia 19104.
NC GM 42415 (NIGMS)
AI 30656 (NIAID)

CA 42909 (NCI)
SO SCIENCE, (1993 Mar 12) 259 (5101) 1622-5.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199306
AB PU.1 recruits the binding of a second B cell-restricted nuclear factor,
NF-EM5, to a DNA site in the ***immunoglobulin*** kappa 3' enhancer.
DNA binding by NF-EM5 requires a protein-protein interaction with PU.1 and
specific DNA contacts. Dephosphorylated PU.1 bound to DNA but did not
interact with NF-EM5. Analysis of serine-to-alanine mutations in PU.1
indicated that serine 148 (Ser148) is required for protein-protein
interaction. PU.1 produced in bacteria did not interact with NF-EM5.
Phosphorylation of bacterially produced PU.1 by purified ***casein***
kinase II modified it to a form that interacted with NF-EM5 and that
recruited NF-EM5 to bind to DNA. Phosphopeptide analysis of bacterially
produced PU.1 suggested that Ser148 is phosphorylated by ***casein***
kinase II. This site is also phosphorylated in vivo. Expression of
wild-type PU.1 increased expression of a reporter ***construct***
containing the PU.1 and NF-EM5 binding sites nearly sixfold, whereas the
Ser148 mutant form only weakly activated transcription. These results
demonstrate that phosphorylation of PU.1 at Ser148 is necessary for
interaction with NF-EM5 and suggest that this phosphorylation can regulate
transcriptional activity.

L12 ANSWER 6 OF 8 MEDLINE
AN 92260636 MEDLINE
DN 92260636
TI Receptor properties of two varicella-zoster virus glycoproteins, gpI and
gpIV, homologous to herpes simplex virus gE and gI.
AU Litwin V; Jackson W; Grose C
CS Department of Microbiology, University of Iowa College of Medicine, Iowa
City 52242..
NC AI22795 (NIAID)
SO JOURNAL OF VIROLOGY, (1992 Jun) 66 (6) 3643-51.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199208
AB The varicella-zoster virus (VZV) genome contains 70 reading frames (ORF),
5 of which encode the glycoproteins gpI, gpII, gpIII, gpIV, and gpV. ORF
67 and 68 lie adjacent to each other in the unique short region of the VZV
genome and code for gpIV and gpI, respectively. These two genes, which are
contained within the HindIII C fragment of the VZV genome, were subcloned
in the correct orientation downstream from the promoter regions of the
eukaryotic expression ***vectors*** pCMV5 and pBJ. After transfection,
5 to 20% of the Cos cells bound antibody specific for the given
glycoprotein. In this study, it was shown that only the cells transfected
with the gpI ***construct*** bound to the Fc fragment of human
immunoglobulin G. Neither the transfected gpIV gene product nor
the ***vector*** only bound to the Fc fragment. Thus, VZV gpI is
confirmed to be the VZV-encoded Fc-binding glycoprotein. Like the
wild-type form of gpI expressed in VZV-infected cells, gpI precipitated
from transfected cells contained both N-linked and O-linked glycans and
was heavily sialated. In addition, the transfected gpI gene product was
phosphorylated both in cell culture and in protein kinase assays by
mammalian ***casein*** kinases I and II. Extensive computer-assisted
analyses of the VZV gpI sequence, as well as those of alphaherpesviral
homolog glycoproteins, disclosed properties similar to those of other cell
surface receptors; these included (i) exocytoplasmic regions rich in
cysteine residues, (ii) membrane-proximal regions with potential O-linked
glycosylation sites, and (iii) cytoplasmic domains with consensus
phosphorylation sites.

L12 ANSWER 7 OF 8 MEDLINE
AN 91060583 MEDLINE
DN 91060583
TI Primary structure of the target of calcium ***vector*** protein of
amphioxus.
AU Takagi T; Cox J A
CS Biological Institute, Faculty of Science, Tohoku University, Sendai,
Japan..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1990 Nov 15) 265 (32) 19721-7.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199103
AB CaVPT, a target protein of Ca2(+)- ***vector*** from amphioxus muscle,
was purified from its complex with CaVP after dissociation by 6 M urea and
chromatographies on DEAE-cellulose and calmodulin-Sepharose. The amino
acid sequence of CaVPT has been determined. The protein is composed of 243
residues and possesses an unblocked N terminus. Its molecular weight is
26,621, distinctly lower than the apparent molecular weight deduced from
electrophoresis on sodium dodecyl sulfate-containing gels. CaVPT contains
a potential Asn-linked glycosylation site, four potential protein kinase C
phosphorylation sites, and two ***casein*** kinase II phosphorylation
sites. From the sequence the following three particular domains can be
inferred: a collagen-like N-terminal segment, rich in Pro and Ala, that
resembles the N-terminal segment of skeletal muscle myosin light chain
kinase; next to it (from residues 33 to 50) is located a strongly
amphiphilic and basic alpha-helical segment which likely binds the calcium
vector protein since a proteolytic cut after Arg50, occurring
occasionally during the purification of CaVPT, impairs the binding to
immobilized calmodulin. This segment is followed by two
immunoglobulin folds. The two ***immunoglobulin*** folds
typically belong to the C2 subclass and particularly resemble those
present in the neural cell surface adhesion molecules NCAM, L1, F11, MAG,
TAG-1, fasciclin II, and amalgam. Recently, the presence of
immunoglobulin folds of this type has been reported in some
intracellular muscular proteins, namely in smooth muscle myosin light
chain kinase, striated muscle C protein and titin, as well as in the
nematode 600-kDa protein twitchin. From this structural study we can
formulate the working hypothesis that CaVPT acts on the structure of the
thick filament in muscle or regulates, perhaps via other
immunoglobulin fold-containing proteins.

L12 ANSWER 8 OF 8 MEDLINE
AN 83164366 MEDLINE
DN 83164366
TI Site-directed point mutation in the src gene oF rous sarcoma virus results
in an inactive src gene product.
AU Bryant D; Parsons J T
NC CA29243 (NCI)
CA27578 (NCI)
SO JOURNAL OF VIROLOGY, (1983 Mar) 45 (3) 1211-6.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-J02351
EM 198307
AB Site-directed mutagenesis techniques were used to ***construct***
defined point mutations within the src gene of the Prague A strain of Rous
sarcoma virus. Bisulfite mutagenesis at a Bg/I restriction site in the src
gene yielded three mutations which contained the same single base change,
a guanine-to-adenine transition. The resulting genomes encoded an src
protein containing a substitution of threonine for alanine at amino acid
position 433. Transfection of chicken cells with mutagenized DNA did not
result in cellular transformation even though the cells produced a
pp60src. Immune complexes containing mutant pp60src did not phosphorylate
immunoglobulin G heavy chain or ***casein*** .

=> d his

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FILE 'MEDLINE' ENTERED AT 16:55:09 ON 04 AUG 1999
L1 4 S IMMUNOGLOBULIN AND WHEY ACIDIC PROTEIN/AB,BI
L2 4 S IMMUNOGLOBULIN# AND WHEY ACIDIC PROTEIN/AB,BI
L3 0 S IMMUNOGLOBULIN# AND BETA-LACTOGLOBULIN PROMOTER/AB,BI
L4 0 S IMMUNOGLOBULIN# AND CASEIN PROMOTER/AB,BI
L5 0 S IMMUNOGLOBULIN# AND BETA-CASEIN PROMOTER/AB,BI
L6 0 S IMMUNOGLOBULIN# AND KAPPA-CASEIN PROMOTER/AB,BI
L7 0 S IMMUNOGLOBULIN# AND LACTALBUMIN PROMOTER/AB,BI
L8 96 S IMMUNOGLOBULIN# AND LACTALBUMIN/AB,BI
L9 0 S L8 AND (CONSTRUCT# OR VECTOR#)/AB,BI
L10 0 S L8 AND TRANSGEN?/AB,BI
L11 190 S IMMUNOGLOBULIN# AND CASEIN/AB,BI
L12 8 S L11 AND (CONSTRUCT# OR VECTOR#)/AB,BI

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COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 7.14 7.29

FILE 'MEDLINE' ENTERED AT 17:05:15 ON 04 AUG 1999

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=> s l1

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L13 13 L1

=> dup rem l13

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L14 6 DUP REM L13 (7 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 6 MEDLINE DUPLICATE 1
AN 1998455664 MEDLINE
DN 98455664
TI Lactogenic immunity in transgenic mice producing recombinant antibodies
neutralizing coronavirus.
AU Castilla J; Sola I; Pintado B; Sanchez-Morgado J M; Enjuanes L
CS Department of Molecular and Cell Biology, Centro Nacional de Biotecnologia, CSIC, Madrid, Spain.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 440 675-86.
Journal code: 2LU. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
EW 19990303
AB Protection against coronavirus infections can be provided by the oral
administration of virus neutralizing antibodies. To provide lactogenic
immunity, eighteen lines of transgenic mice secreting a recombinant IgG1
monoclonal antibody (rIgG1) and ten lines of transgenic mice secreting
recombinant IgA monoclonal antibodies (rIgA) neutralizing transmissible
gastroenteritis coronavirus (TGEV) into the milk were generated. Genes
encoding the light and heavy chains of monoclonal antibody (MAb) 6A.C3
were expressed under the control of regulatory sequences derived from the
mouse genomic DNA encoding the ***whey*** ***acidic*** ***protein*** (WAP) and beta-lactoglobulin (BLG), which are highly
abundant milk proteins. The MAb 6A.C3 binds to a highly conserved epitope
present in coronaviruses of several species. This MAb does not allow the
selection of neutralization escaping virus mutants. The antibody was
expressed in the milk of transgenic mice with titers of one million as
determined by RIA, and neutralized TGEV infectivity by one million fold
corresponding to ***immunoglobulin*** concentrations of 5 to 6 mg per
ml. Matrix attachment regions (MAR) sequences were not essential for rIgG1
transgene expression, but co-microinjection of MAR and antibody genes led
to a twenty to ten thousand-fold increase in the antibody titer in 50% of
the rIgG1 transgenic animals generated. Co-microinjection of the genomic
BLG gene with rIgA light and heavy chain genes led to the generation of
transgenic mice carrying the three transgenes. The highest antibody titers
were produced by transgenic mice that had integrated the antibody and BLG
genes, although the number of transgenic animals generated does not allow

a definitive conclusion on the enhancing effect of BLG co-integration.
Antibody expression levels were transgene copy number independent and
integration site dependent. The generation of transgenic animals producing
virus neutralizing antibodies in the milk could be a general approach to
provide protection against neonatal infections of the enteric tract.

L14 ANSWER 2 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1998119750 EMBASE
TI Engineering passive immunity in transgenic mice secreting virusneutralizing antibodies in milk.
AU Castilla J.; Pintado B.; Sola I.; Sanchez-Morgado J.M.; Enjuanes L.
CS L. Enjuanes, Department of Molecular/Cell Biology, Centro Nacional de
Biotecnologia, Consejo Superior Invest. Cientificas, Cantoblanco, 28049
Madrid, Spain. L.Enjuanes@cnb.uam.es
SO Nature Biotechnology, (1998) 16/4 (349-354).
Refs: 42
ISSN: 1087-0156 CODEN: NABIF
CY United States
DT Journal; Article
FS 004 Microbiology
007 Pediatrics and Pediatric Surgery
026 Immunology, Serology and Transplantation
LA English
SL English
AB Protection against enteric infections can be provided by the oral administration of pathogen-neutralizing antibodies. To provide passive
immunity, 18 lines of transgenic mica secreting a recombinant mono-clonal
antibody (Mab) neutralizing transmissible gastroenteritis coronavirus
(TGEV) into the milk were generated. The genes encoding a chimeric Mab
with the variable modules of the murine TGEV-specific Mab 6A.C3 and the
constant modules of a human IgG, isotype Mab were expressed under the
control of regulatory sequences derived from the ***whey*** ***acidic*** ***protein*** , which is an abundant milk protein. The
Mab 6A.C3 binds to a highly conserved epitope present in coronaviruses of
several species, which does not allow the selection of neutralization
escape mutants. Antibody expression titers of 104 were obtained in the
milk of transgenic mice that reduced TGEV infectivity 104-fold. The
antibody was synthesized at high levels throughout lactation. Integration
of matrix attachment region sequences with the antibody genes led to a 20-
to 10,000-fold increase in the antibody titer in 50% of the transgenic
animals. Antibody expression levels were transgene copy number independent
and related to the site of integration. The generation of transgenic
animals producing virus neutralizing antibodies in milk could provide an
approach to protection against neonatal infections of the enteric tract.

L14 ANSWER 3 OF 6 MEDLINE DUPLICATE 2
AN 95358828 MEDLINE
DN 95358828
TI The effect of various introns and transcription terminators on the efficiency of expression vectors in various cultured cell lines and in the
mammary gland of transgenic mice.
AU Petitclerc D; Attal J; Theron M C; Bearzotti M; Bolifraud P; Kann G;
Stinnakre M G; Pointu H; Puissant C; Houdebine L M
CS Agriculture et Agro-Alimentaire Canada, Est Lennoxville, Quebec.
SO JOURNAL OF BIOTECHNOLOGY, (1995 Jun 21) 40 (3) 169-78.
Journal code: AL6. ISSN: 0168-1656.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; B
EM 199511
AB Various combinations of promoters, introns and transcription terminators
were used to drive the expression of bovine growth hormone (bGH) cDNA in
different cell types. In constructs containing the human cytomegalovirus
(hCMV) promoter and the SV40 late genes terminator, the intron from SV40
genes (VP1) was much more efficient, than the intron from the early genes
(t). The synthetic intron SIS generated by the association of an
adenovirus splice donor and an ***immunoglobulin*** G splice acceptor
showed the highest activity. The respective potency of these introns was
similar in several mammalian (CHO, HC11 and COS) and fish (TO2 and EPC)
cells. The rabbit ***whey*** ***acidic*** ***protein*** (WAP)
gene promoter was highly efficient to drive the expression of bGH gene in
the HC11 mammary cell lines. In contrast, the bGH cDNA under the control
of the same promoter was much less efficiently expressed when the SV40 VP1
intron and transcription terminator were used. The rabbit WAP gene and the
human GH gene terminators did not or only moderately enhanced the
expression of the construct WAP bGH cDNA. Introduction of a promoter
sequence from the mouse mammary tumor virus (MMTV) LTR in the VP1 intron
increased very significantly the expression of the WAP bGH cDNA. Although
several of these vectors showed high potency when expressed stably in HC11
cells, all of them were only moderately efficient in transgenic mice.
These data indicate that the VP1 and the SIS introns may be used to
express foreign cDNAs with good efficiency in different cell types. The
addition of an enhancer within an intron may still reinforce its
efficiency. However, transfection experiments, even when stable expression
is carried out, are poorly predictive of the potential efficiency of a
vector in transgenic animals.

L14 ANSWER 4 OF 6 MEDLINE DUPLICATE 3
AN 1998040670 MEDLINE
DN 98040670
TI Production of active anti-CD6 mouse/human chimeric antibodies in the milk
of transgenic mice.
AU Limonta J; Pedraza A; Rodriguez A; Freyre F M; Barral A M; Castro F O;
Lleonart R; Gracia C A; Gavilondo J V; de la Fuente J
CS Mammalian Cell Genetics Division, Center for Genetic Engineering and
Biotechnology, Havana, Cuba.
SO IMMUNOTECHNOLOGY, (1995 Aug) 1 (2) 107-13.
Journal code: CR0. ISSN: 1380-2933.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
EW 19980302
AB The expression of chimeric genes in the mammary gland of transgenic farm
animals has become an alternative for the large-scale production of recombinant proteins and for the modification of milk composition. In this
paper, we show that a mouse/human chimeric antibody against the human CD6
leukocyte antigen can be assembled and correctly folded by the mammary
gland, and secreted to milk, where it maintains its specificity. The base
sequences encoding for the heavy and light chain variable regions of the
anti-CD6 mouse monoclonal antibody IOR-T1 were cloned by the

polymerase
chain reaction from hybridoma cDNA, coupled to human heavy and light chain
constant region genes, and inserted in a vector containing the 5' regulatory region of the rabbit ***whey*** ***acidic*** ***protein*** gene. Transgenic mice were produced by conventional
pronuclei microinjection techniques. Integration and transgene copy number
were determined by Southern blot. Assembled human ***immunoglobulin***
was detected in milk using a sandwich ELISA. Expression levels of chimeric
antibodies in milk were determined to be around 400 micrograms/ml by
Western blot, using CHO-derived chimeric IOR-T1 antibodies as reference.
The chimeric antibodies produced in milk recognized human peripheral blood
T lymphocytes by indirect immunofluorescence, with the classical patch-like pattern of IOR-T1.

L14 ANSWER 5 OF 6 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:342690 BIOSIS
DN PREV199396039690
TI A novel gene product associated with mu chains in immature B cells.
AU Shirasawa, Takuji; Ohnishi, Kazuo; Hagiwara, Shinji; Shigemoto, Kazuhiro;
Takebe, Yutaka; Rajewsky, Klaus; Takemori, Toshitada (1)
CS (1) Dep. Immunol., NIH, Tokyo Japan
SO EMBO (European Molecular Biology Organization) Journal, (1993) Vol. 12,
No. 5, pp. 1827-1834.
ISSN: 0261-4189.
DT Article
LA English
AB A previously unreported B cell specific gene, which we have named 8HS-20,
was isolated from the cDNA library of a pre-B cell clone by subtraction
and differential hybridization. This gene is selectively expressed as a
0.75 kb transcript in pre-B and bone marrow-derived B cell lines; a
transcript of the same size is also found in bone marrow and, albeit at
low levels, in spleen. The deduced amino acid sequence of the 8HS-20 cDNA
displayed homology to a B cell specific gene, VpreB-1, and to members of
the ***immunoglobulin*** supergene family including V-lambda, V-kappa,
V-H, TCRV-alpha, V-beta and CD8. Biochemical analysis using purified
antiserum against 8HS-20 oligopeptides indicates that the gene encodes
proteins with mol. wts of 13.5, 14, 15.5 and 16 kDa, which associate with
mu chains in pre-B cell lines, and that these molecules are expressed
concomitantly with VpreB-1 and lambda-5 gene products in the same cell
lines.

L14 ANSWER 6 OF 6 MEDLINE DUPLICATE 4
AN 93173503 MEDLINE
DN 93173503
TI T1, an ***immunoglobulin*** superfamily member, is expressed in
H-ras-dependent epithelial tumours of mammary cells.
AU Rossler U; Andres A C; Reichmann E; Schmahl W; Werenskiold A K
CS Department of Cell Chemistry, GSF-Forschungszentrum fur Umwelt und
Gesundheit, Neuherberg, Germany..
SO ONCOGENE, (1993 Mar) 8 (3) 609-17.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199305
AB T1 is a glycosylated protein in the carcinoembryonic antigen (CEA) family
of tumour marker molecules. It was originally identified by virtue of its
transient induction after the expression of p21H-ras in NIH3T3
fibroblasts. Here we show that the T1 gene is activated in mammary
adenocarcinomas of transgenic mice harbouring an H-ras transgene under the
control of the mammary-specific ***whey*** ***acidic*** ***protein*** (WAP) promoter. By contrast, T1 mRNA was not, or only
faintly, detectable in mammary carcinomas of transgenic mice bearing a
WAP-myc transgene. Thus, T1 overexpression does not appear to be a general
tumour-specific phenomenon. A dependence of T1 gene expression on the
action of p21H-ras is suggested by the observation of T1 mRNA in nude
mouse tumours generated from H-ras-transformed cultured mammary epithelial
cells. Interestingly, activation of the T1 gene is also found during the
maturation of the mammary gland (3-4 weeks after birth), whereas it is
absent during its terminal differentiation in pregnancy and lactation.
This expression pattern suggests a role for the secreted T1 glycoprotein
in the phase of epithelial proliferation of the mammary gland. It appears
that p21H-ras-induced transformation of mammary epithelial cells mimics
the situation occurring in puberty. In both developmental stages the T1
glycoprotein might affect cell interactions of the proliferating
epithelial cells with the surrounding stroma. It might thus promote ductal
outgrowth in gland maturation as well as invasive growth of
p21H-ras-transformed mammary epithelial cells.

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L15 23 L2

=> s l2 not l1

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'AB' IS NOT A VALID FIELD CODE
L16 10 L2 NOT L1

=> dup rem l16

PROCESSING COMPLETED FOR L16
L17 10 DUP REM L16 (0 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L17 ANSWER 1 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1998:696460 CAPLUS
DN 130:108924
TI Lactogenic immunity in transgenic mice producing recombinant antibodies
neutralizing coronavirus
AU Catilla, J.; Sola, I.; Pintado, B.; Sanchez-Morgado, J. M.; Enjuanes, L.
CS Department of Molecular and Cell Biology Centro Nacional de Biotecnologia,
CSIC Campus Universidad Autonoma, Madrid, 28049, Spain
SO Adv. Exp. Med. Biol. (1998), 440(Coronaviruses and Arteriviruses), 675-686
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Publishing Corp.
DT Journal
LA English
AB Protection against coronavirus infections can be provided by the oral
administration of virus neutralizing antibodies. To provide lactogenic
immunity, eighteen lines of transgenic mice secreting a recombinant IgG1

monoclonal antibody (rIgG1) and ten lines of transgenic mice secreting
recombinant IgA monoclonal antibodies (rIgA) neutralizing transmissible
gastroenteritis coronavirus (TGEV) into the milk were generated. Genes
encoding the light and heavy chains of monoclonal antibody (MAb) 6A.C3
were expressed under the control of regulatory sequences derived from the
mouse genomic DNA encoding the ***whey*** ***acidic*** ***protein*** (WAP) and beta-lactoglobulin (BLG), which are highly
abundant milk proteins. The MAb 6A.C3 binds to a highly conserved epitope
present in coronaviruses of several species. This MAb does not allow the
selection of neutralization escaping virus mutants. The antibody was
expressed in the milk of transgenic mice with titers of one million as
detd. by RIA, and neutralized TGEV infectivity by one million fold
corresponding to Ig concns. of 5 to 6 mg per mL. Matrix attachment
regions (MAR) sequences were not essential for rIgG1 transgene expression,
but co-microinjection of MAR and antibody genes led to a twenty to ten
thousand-fold increase in the antibody titer in 50% of the rIgG1
transgenic animals generated. Co-microinjection of the genomic BLG gene
with rIgA light and heavy chain genes led to the generation of transgenic
mice carrying the three transgenes. The highest antibody titers were
produced by transgenic mice that had integrated the antibody and BLG
genes, although the no. of transgenic animals generated does not allow a
definitive conclusion on the enhancing effect of BLG co-integration.
Antibody expression levels were transgene copy no. independent and
integration site dependent. The generation of transgenic animals
producing virus neutralizing antibodies in the milk could be a general
approach to provide protection against neonatal infections of the enteric
tract.

L17 ANSWER 2 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1997:650467 CAPLUS
DN 127:315589
TI Cytochrome P450 encoding retroviral vectors and their use as antitumor
agents
IN Gunzburg, Walter H.; Karle, Peter; Saller, Robert Michael
PA Bavarian Nordic Research Institute A/S, Den.; GSF-Forschungszentrum Fur
Umwelt Und Gesundheit; Gunzburg, Walter H.; Karle, Peter; Saller, Robert
Michael
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9735994	A2	19971002	WO 1997-EP1585	19970327
WO 9735994	A3	19971120		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9723827	A1	19971017	AU 1997-23827	19970327
EP 892852	A2	19990127	EP 1997-919307	19970327

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

NO 9804540	A	19980928	NO 1998-4540	19980928

PRAI DK 1996-352 19960327
WO 1997-EP1585 19970327
AB A replication-defective retroviral vector carrying a cytochrome P 450 gene
under transcriptional control of target cell specific regulatory elements
or promoters, or X-ray inducible promoters is disclosed.

L17 ANSWER 3 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1997:18384 CAPLUS
DN 126:43610
TI Animal gene therapy expression cassettes and DNA constructs for treatment
of infectious diseases
IN Gagne, Marc
PA Immunova, Can.; Gagne, Marc
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9635793	A1	19961114	WO 1996-CA297	19960510

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

CA 2220472	AA	19961114	CA 1996-2220472	19960510
AU 9656416	A1	19961129	AU 1996-56416	19960510
EP 828839	A1	19980318	EP 1996-913403	19960510

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 11505113	T2	19990518	JP 1996-533627	19960510

PRAI GB 1995-9461 19950510
WO 1996-CA297 19960510
AB The present invention relates to DNA sequences, expression cassettes and
DNA constructs for use in therapy, specifically in gene therapy for the
treatment of infectious diseases such as mastitis. Also included are
pharmaceutical and veterinary compns. contg. the constructs, and cells
which have been transformed with the DNA and which are suitable for
implantation into a host mammal. The gene therapy of infectious diseases
can be effected in situ in targeted tissue or systemically.

L17 ANSWER 4 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1997:6067 CAPLUS
DN 126:27673
TI Transgenic multicellular eukaryotes expressing genes for enzymes of
post-translational modification of proteins
IN Lubon, Henryk; Drohan, William N.; Paleyanda, Rekha K.
PA American Red Cross, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9634966	A2	19961107	WO 1996-US6121	19960506

W: AU, CA, JP, MX
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
CA 2220109 AA 19961107 CA 1996-2220109 19960506
AU 9663474 A1 19961121 AU 1996-63474 19960506
PRAI US 1995-434834 19950504
WO 1996-US6121 19960506
AB Transgenic non-human multicellular organisms contg. expression cassettes
for enzyme involved in post-translational modification of proteins are
described for use in the manuf. of proteins. The transgenic organism most
often carries genes for enzymes of post-translational modification and the
gene for a protein of interest that is a substrate for the modification
enzyme. Preferably, the genes are regulated, e.g. by development,
tissue-type, or by a chem. inducer and the modified protein is secreted
into a bodily fluid. An example provides transgenic mice that synthesize
human protein C and the processing protease PACE/furin in mammary glands
and secrete both proteins into milk. The genes are placed under control
of the mammary gland-specific promoter of the ***whey*** ***acidic*** ***protein*** gene.

L17 ANSWER 5 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1996:661119 CAPLUS
DN 125:294771
TI Viral and plasmid vectors encoding mouse mammary tumor virus Naf repressor
or Sag antigen for control of viral infections or lymphocyte gene therapy
IN Guenzburg, Walter H.; Salmons, Brian
PA Bavarian Nordic Research Institute A/s, Den.; GSF-Forschungszentrum fuer
Umwelt und Gesundheit GmbH
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9628564	A1	19960919	WO 1996-EP1002	19960308

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS,
JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG,
US, UZ
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG
AU 9651040 A1 19961002 AU 1996-51040 19960308
EP 817859 A1 19980114 EP 1996-907399 19960308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI
JP 11508441 T2 19990727 JP 1996-527260 19960308
PRAI DK 1995-244 19950309
WO 1996-EP1002 19960308
AB The invention refers to novel recombinant vectors useful for gene therapy
of viral infections and of diseases assocd. with B and T cells. The
present invention relates, furthermore, to novel usages of the two
products of the open reading frame of mouse mammary tumor virus, i.e. the
transcription repressor Naf and superantigen Sag. Procon (promoter
conversion) viral vectors may be used to deliver the Naf gene to target
cells and thereby repress expression from heterologous viral promoters.
Alternatively, the vector may deliver the Sag gene, and, optionally, a B-
or T-cell-specific therapeutic gene. This will stimulate expansion of B
and T cells expressing the therapeutic gene.

L17 ANSWER 6 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1996:661120 CAPLUS
DN 125:294754
TI Vectors carrying therapeutic genes encoding antimicrobial peptides for
gene therapy
IN Guenzburg, Walter H.; Winder, David; Saller, Robert Michael
PA Bavarian Nordic, Den.; GSF-Forschungszentrum fuer Umwelt und Gesundheit
GmbH
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9628563	A1	19960919	WO 1996-EP1001	19960308

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS,
JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG,
US, UZ
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG
AU 9651039 A1 19961002 AU 1996-51039 19960308
EP 817858 A1 19980114 EP 1996-907398 19960308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI
JP 11503305 T2 19990326 JP 1996-527259 19960308
PRAI DK 1995-243 19950309
WO 1996-EP1001 19960308
AB The present invention relates to retroviral vectors carrying sequences
encoding naturally occurring, antimicrobial peptides or derivs. thereof
for the treatment of mammalian tumors, viral infections such as HIV
infection and bacterial and fungal infections. In particular the present
invention relates to retroviral vectors which undergo promoter conversion
(Procon vectors) carrying such sequences. Since these vectors also carry
tumor or virus specific regulatory elements, the therapeutic antimicrobial
peptide will be delivered and expressed only in relevant, affected cells
and not in innocent bystander cells. The U3 region of murine leukemia
virus-derived vector BAG was replaced with a mouse mammary tumor virus U3
region without the inverted repeats but contg. the promoter, a region
conferring responsiveness to glucocorticoid hormones, and a region contg.
an element directing expression to the mammary gland. A preprocecropin A
gene was inserted next to the promoter to produce vector p125.CercA. EJ
cells expressing the luciferase gene fused to the HIV LTR and the Tat gene
displayed luciferase expression. When these recombinant cells were
infected with p125.CercA there was little luciferase expression.

L17 ANSWER 7 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1996:346074 CAPLUS
DN 125:2982
TI Safe, non-self-inactivating retroviral expression vectors using non-LTR
promoters for gene therapy
IN Guenzburg, Walter Henry; Saller, Robert Michael
PA GSF-Forschungszentrum fuer Umwelt und Gesundheit GmbH, Germany
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9607748	A1	19960314	WO 1995-EP3445	19950901

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2198210	AA	19960314	CA 1995-2198210	19950901
AU 9535201	A1	19960327	AU 1995-35201	19950901
AU 688590	B2	19980312		
EP 779929	A1	19970625	EP 1995-931969	19950901

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

CN 1159210	A	19970910	CN 1995-194903	19950901
BR 9508664	A	19980106	BR 1995-8664	19950901
HU 76974	A2	19980128	HU 1997-1764	19950901
JP 10507628	T2	19980728	JP 1995-509186	19950901
NO 9700902	A	19970424	NO 1997-902	19970227
FI 9700892	A	19970228	FI 1997-892	19970228

PRAI DK 1994-1017 19940902
WO 1995-EP3445 19950901

AB Retroviral expression vectors for gene therapy with a reduced risk of recombination with helper virus genomes and that use non-retroviral promoters in place of the LTRs are described. These vectors are constructed with non-retroviral regulatory elements in place of the 3'-LTR. After infection, the 3'-LTR region is duplicated and transposed to the 5'-LTR leading to elimination of the viral LTR and expression of the gene from the 5'-LTR. The construct replaces the U3 region of the 3'-LTR with the foreign promoter. This vector will not self-inactivate over time. Vectors using the promoter of the ***whey*** ***acidic*** ***protein*** gene or of the mouse mammary tumor virus to direct mammary gland-specific expression of a .beta.-galactosidase gene are demonstrated.

L17 ANSWER 8 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1995:994888 CAPLUS
DN 124:47632
TI Manufacture and secretion into milk of oligosaccharides and glycoconjugates typical of human milk by mammary gland-specific expression of the human genes for oligosaccharide biosynthetic enzymes
IN Prieto, Pedro Antonio; Smith, David Fletcher; Cummings, Richard Dale; Kopchik, John Joseph; Mukerji, Pradip; Moremen, Kelley Wilson; Pierce, James Michael
PA Abbott Laboratories, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9524495	A1	19950914	WO 1995-US967	19950124

W: AU, CA, FI, JP, MX, NL, NZ
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 5750176	A	19980512	US 1994-208889	19940309
CA 2184686	AA	19950914	CA 1995-2184686	19950124
AU 9516901	A1	19950925	AU 1995-16901	19950124
AU 697523	B2	19981008		
EP 750673	A1	19970102	EP 1995-908663	19950124

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE

JP 09510094	T2	19971014	JP 1995-523443	19950124

PRAI US 1994-208889 19940309
WO 1995-US967 19950124

AB Methods for genetic engineering of the milk of a non-human mammal is characterized so that it contains heterologous components produced as the secondary gene products of a heterologous gene integrated into the genome of the transgenic non-human mammal are described. The heterologous gene encodes an enzyme such as a human enzyme selected from the group consisting of glycosyltransferases, phosphorylases, hydroxylases, peptidases and sulfotransferases. Esp. useful in the practice of the invention are human glycosyltransferases. The desired heterologous components include oligosaccharides, glycoconjugates. The oligosaccharides and glycoconjugates may be isolated from the milk of the transgenic mammals and used in the prepn. of pharmaceuticals, diagnostic kits, nutritional products and the like. The whole milk may also be used to formulate nutritional products that provide special advantages. The transgenic milk may also be used in the prodn. of specialized enteral nutritional products. Methods for transforming oocytes and screening preimplantation embryos for the presence of the transforming DNA are described. The cloning and expression of a cDNA for a human fucosyltransferase in transgenic mice using the ***whey*** ***acidic*** ***protein*** gene promoter to direct mammary gland-specific expression in mice is demonstrated.

L17 ANSWER 9 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1995:780439 CAPLUS
DN 123:190527
TI Transgenic production of antibodies in milk and usefulness for diagnostics, therapy, or industry
IN Meade, Harry; Ditullio, Paul; Pollock, Daniel
PA Genzyme Transgenics Corp., USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9517085	A1	19950629	WO 1994-US14795	19941220

W: AU, CA, JP, NZ
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 5827690	A	19981027	US 1993-170579	19931220
CA 2178941	AA	19950629	CA 1994-2178941	19941220
AU 9515172	A1	19950710	AU 1995-15172	19941220
AU 688845	B2	19980319		
EP 741515	A1	19961113	EP 1995-906691	19941220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 09506779	T2	19970708	JP 1994-517602	19941220
US 5849992	A	19981215	US 1995-410887	19950327
AU 9873079	A1	19980820	AU 1998-73079	19980619

PRAI US 1993-170579 19931220
WO 1994-US14795 19941220

AB A method for the prodn. of monoclonal antibodies in mammal's milk, through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

L17 ANSWER 10 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1993:230822 CAPLUS
DN 118:230822
TI Protein composition of rhesus monkey milk: comparison to human milk
AU Kunz, Clemens; Lonnerdal, Bo
CS Dep. Nutr., Univ. California, Davis, CA, 95616, USA
SO Comp. Biochem. Physiol., A: Comp. Physiol. (1993), 104A(4), 793-7
CODEN: CBPAB5; ISSN: 0300-9629

DT Journal
LA English
AB Proteins in human milk and Rhesus monkey milk were compared by FPLC gel
filtration and anion-exchange chromatog., SDS-PAGE, nitrogen and protein
detn. Mature Rhesus milk is higher in protein concn. (15-20 mg/mL) than
human milk (8-9 mg/mL). Non-protein nitrogen is 6-13% in Rhesus milk but
25-30% in human milk. Secretory IgA, lactoferrin, serum albumin, .alpha.-lactalbumin and lysozyme are present in Rhesus milk, but at a
lower concn. than in human milk. The casein subunit pattern is more
complex in Rhesus milk compared to human milk. The ratio of whey proteins
to casein is similar in both milks (.apprxeq.60/40). A protein with a Mr
of 21,600 is a major component in monkey whey but is not found in human
milk.

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L18 2 L4

=> dup rem l18

PROCESSING COMPLETED FOR L18
L19 2 DUP REM L18 (0 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L19 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN 1991:625431 CAPLUS
DN 115:225431
TI Production of heterologous polypeptides by recombinant cattle and
transgenic methods
IN Heyneker, Herbert L.; Deboer, Herman A.; Strijker, Rein; Plantenburg,
Gerard; Lee, Sang He
PA Genpharm International, Inc., USA
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9108216	A1	19910613	WO 1990-US6874	19901130
W: AU, BR, CA, FI, JP, KR, LK, MC, NO, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2075206	AA	19910602	CA 1990-2075206	19901130
AU 9169608	A1	19910626	AU 1991-69608	19901130
AU 656720	B2	19950216		
EP 502976	A1	19920916	EP 1991-901026	19901130
EP 502976	B1	19960703		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 140027	E	19960715	AT 1991-901026	19901130
EP 737746	A2	19961016	EP 1995-203326	19901130
EP 737746	A3	19961023		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2090299	T3	19961016	ES 1991-901026	19901130
RU 2095414	C1	19971110	RU 1990-5052392	19901130
CN 1053446	A	19910731	CN 1990-109733	19901201
NO 9202996	A	19920729	NO 1992-2996	19920729
FI 9203485	A	19920731	FI 1992-3485	19920731
US 5633076	A	19970527	US 1993-154019	19931116
US 5741957	A	19980421	US 1995-461333	19950605
PRAI US 1989-444745		19891201		
US 1990-619131		19901127		
EP 1991-901026		19901130		
WO 1990-US6874		19901130		
US 1992-898956		19920615		
US 1993-77788		19930615		
US 1993-154019		19931116		

AB A method for prepg. transgenic cows which secrete recombinant proteins
into their milk is described. The gene to be expressed in mammary tissue
is fused to a mammary tissue-specific promoter, e.g. that of the casein
gene, a signal sequence, and a 3' flanking sequence functional in cattle.
The chimeric gene is first methylated, e.g. by cloning it in a prokaryotic
host. Fertilized oocytes are then transformed with this gene, and the
fertilized oocytes are cultured to the preimplantation embryo stage. A
cell is removed from the embryo to test for the presence of the desired
gene: the chimeric methylated gene is resistant to restriction
endonuclease cleavage. The hemiembryo remaining after removing the cell
is cloned to prep. multiple embryos which are implanted into a cow to
produce transgenic offspring. The milk from the transgenic cows can be
used in food formulations, esp. infant formulas. A chimeric gene
comprising human lactoferrin cDNA flanked by bovine .alpha.S1-***casein*** ***promoter*** and signal sequence and 3' regions was
prepd. Transgenic cows secreting lactoferrin into their milk were
produced using this gene according to the above procedure.

L19 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN 1989:451714 CAPLUS
DN 111:51714
TI Manufacture of recombinant proteins by secretion into milk of transgenic
mammals
IN Meade, Harry; Longberg, Nils
PA Biogen N. V., Neth.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 8810118	A1	19881229	WO 1988-US2134	19880623
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4873316	A	19891010	US 1987-65994	19870623
EP 347431	A1	19891227	EP 1988-906454	19880623
EP 347431	B1	19951004		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02500798	T2	19900322	JP 1988-505800	19880623
AT 128625	E	19951015	AT 1988-906454	19880623
US 5750172	A	19980512	US 1995-460959	19950605
PRAI US 1987-65994		19870623		
WO 1988-US2134		19880623		
US 1989-332293		19890331		
US 1993-109865		19930820		
US 1994-322984		19941014		

AB A method for producing desired proteins by producing transgenic mammals
which secrete the protein into the milk is described. A section of the
bovine .alpha. S-1 casein gene contg. the promoter and signal sequence was
cloned. This DNA sequence was ligated to tissue-type plasminogen
activator (tPA) cDNA via DNA contg. RNA processing splice sites (which
allow the casein signal sequence RNA to be spliced to the tPA-encoding
RNA) to prep. pCAS1151. Preimplantation fertilized mice embryos were
microinjected with this (linearized) DNA and then implanted in
pseudopregnant female mice. Of 262 embryos injected and implanted, 23
live pups were born, 5 of which contained the desired DNA sequences. Male

G0 mice were bred with females. Females of the G1 progeny which contained
the tPA sequence produced 0.2-0.5 .mu.g tPA/mL milk.

=> s immunoglobulin# and beta-lactoglobulin/ab,bi

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L20 909 IMMUNOGLOBULIN# AND BETA-LACTOGLOBULIN/AB,BI

=> s l20 and promoter#/ab,bi

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'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L21 2 L20 AND PROMOTER#/AB,BI

=> dup rem l21

PROCESSING COMPLETED FOR L21
L22 2 DUP REM L21 (0 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L22 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN 1999:77669 CAPLUS
DN 130:134970
TI Heterologous expression of proteins by rescued vector comprising an intron
IN Colman, Alan; Garner, Ian; Dalrymple, Michael Alexander
PA PPL Therapeutics (Scotland) Limited, UK
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9903981	A1	19990128	WO 1998-GB2130	19980717

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9884502 A1 19990210 AU 1998-84502 19980717
PRAI GB 1997-15064 19970717
WO 1998-GB2130 19980717
AB A nucleic acid expression construct comprising: (a) a ***promoter*** ;
(b) an intron whose natural position is within the 5'-untranslated region
of a gene from which it is derived; (c) a coding sequence; and (d) a
3'-flanking sequence wherein the intron (b) is not derived from the same
gene as that from which either the ***promoter*** (a) or the
protein-coding sequence (c) is derived and processes, vectors, hosts and
uses involving such a construct to obtain inter alia an increase in the
level of expression of the coding sequence. To take advantage of "rescue"
technol., a pMAD vector was constructed from the ovine . ***beta*** .-
lactoglobulin gene for the cloning of cDNAs. The vector contains
the same 5' and 3' flanking sequences preseng in the . ***beta*** .-
lactoglobulin gene which itself always gives rise to high level
expression in transgenic mice, but lacks all coding sequences and introns
of the intact genes. Cloning of cDNAs in the unique EcoRV site between 5'
and 3' flanking sequences results in constructs suitable for expression by
the "rescue" approach. If instead of the . ***beta*** .-
lactoglobulin first intron, an intron whose natural position is
within the 5'-untranslated region of its gene is used (e.g., the bovine or
ovine .beta.-casein intron 1 or the cardiac actin intron 1), good
expression results. The expression constructs are exemplified for the
expression of protein C, antibody fragments, IgG, adhesion mol., and
collagen.

L22 ANSWER 2 OF 2 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1999:188239 BIOSIS
DN PREV199900188239
TI Variable immune response against a developmentally regulated self-antigen.
AU Steinhoff, U. (1); Maloy, K. J.; Burkhart, C.; Clark, A. J.; Ruelicke, T.;
Hengartner, H.; Zinkernagel, R. M.
CS (1) Max-Planck Institute for Infection Biology, Monbijoustr. 2, 10117,
Berlin Germany
SO Journal of Autoimmunity, (Feb., 1999) Vol. 12, No. 1, pp. 27-34.
ISSN: 0896-8411.
DT Article
LA English
AB We studied the reactivity of T and B cells against a soluble form of the
glycoprotein of vesicular stomatitis virus (VSV-G) which was expressed in
a transgenic mouse (line 23) under the control of the hormone regulated
beta - ***lactoglobulin*** ***promoter*** . Transgenic mice
expressed VSV-G in the thymus, spleen, mammary gland and lung. VSV-G
transcripts in the thymus varied with age, i.e., expression was high early
in life and decreased with age. VSV-G transgenic mice immunized with
recombinant vaccinia virus expressing VSV-G exhibited normal
VSV-G-specific IgM levels, but a 30-fold reduction in IgG response,
indicating functional VSV-G-specific B cell activity but impaired T helper
cell responses. Interestingly, VSV-G-specific T helper cell activity was
reduced only early (4-10 weeks) and late in life (>40 weeks) but was
normal in between. Double transgenic mice expressing VSV-G and a
VSV-G-specific TCR (line 23 X 7) demonstrated that TCR transgenic CD4+ T
cells were partially deleted in earlylife, but then gradually repopulated
the periphery and remained constant. These findings suggest that in line
23 two different mechanisms regulated levels of the immune response:
clonal reduction/deletion of VSV-G-specific T cells during early life
followed by peripheral anergy at a later stage.

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L23 1345 L11

=> s l23 and promoter#/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE

'AB' IS NOT A VALID FIELD CODE
L24 24 L23 AND PROMOTER#/AB,BI

=> dup rem l24

PROCESSING COMPLETED FOR L24
L25 13 DUP REM L24 (11 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L25 ANSWER 1 OF 13 CAPLUS COPYRIGHT 1999 ACS
AN 1999:77669 CAPLUS
DN 130:134970
TI Heterologous expression of proteins by rescued vector comprising an intron
IN Colman, Alan; Garner, Ian; Dalrymple, Michael Alexander
PA PPL Therapeutics (Scotland) Limited, UK
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
--- --- --- --- ---
PI WO 9903981 A1 19990128 WO 1998-GB2130 19980717
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9884502 A1 19990210 AU 1998-84502 19980717
PRAI GB 1997-15064 19970717
WO 1998-GB2130 19980717
AB A nucleic acid expression construct comprising: (a) a ***promoter*** ;
(b) an intron whose natural position is within the 5'-untranslated region
of a gene from which it is derived; (c) a coding sequence; and (d) a
3'-flanking sequence wherein the intron (b) is not derived from the same
gene as that from which either the ***promoter*** (a) or the
protein-coding sequence (c) is derived and processes, vectors, hosts and
uses involving such a construct to obtain inter alia an increase in the
level of expression of the coding sequence. To take advantage of "rescue"
technol., a pMAD vector was constructed from the ovine
.beta.-lactoglobulin gene for the cloning of cDNAs. The vector contains
the same 5' and 3' flanking sequences preseng in the .beta.-lactoglobulin
gene which itself always gives rise to high level expression in transgenic
mice, but lacks all coding sequences and introns of the intact genes.
Cloning of cDNAs in the unique EcoRV site between 5' and 3' flanking
sequences results in constructs suitable for expression by the "rescue"
approach. If instead of the .beta.-lactoglobulin first intron, an intron
whose natural position is within the 5'-untranslated region of its gene is
used (e.g., the bovine or ovine .beta.- ***casein*** intron I or the
cardiac actin intron 1), good expression results. The expression
constructs are exemplified for the expression of protein C, antibody
fragments, IgG, adhesion mol., and collagen.

L25 ANSWER 2 OF 13 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97257933 EMBASE
DN 1997257933
TI Distinct functional properties of I.kappa.B.alpha. and I.kappa.B.beta..
AU Tran K.; Merika M.; Thanos D.
CS D. Thanos, DBMB, Columbia University, 630 West 168th St, New York, NY
10032, United States
SO Molecular and Cellular Biology, (1997) 17/9 (5386-5399).
Refs: 65
ISSN: 0270-7306 CODEN: MCEBD4
CY United States
DT Journal; Article
FS 004 Microbiology
LA English
SL English
AB The biological activity of the transcription factor NF-.kappa.B is
controlled mainly by the I.kappa.B.alpha. and I.kappa.B.beta. proteins,
which restrict NF-.kappa.B to the cytoplasm and inhibit its DNA binding
activity. Here, we carried out e experiments to determine and compare the
mechanisms by which I.kappa.B.alpha. and I.kappa.B.beta. inhibit
NF-.kappa.B-dependent transcriptional activation. First, we found that in
vivo I.kappa.B.alpha. is a stronger inhibitor of NF-.kappa.B than is
I.kappa.B.beta.. This difference is directly correlated with their
abilities to inhibit NF-.kappa.B binding to DNA in vitro and in vivo.
Moreover, I.kappa.B.alpha., but not I.kappa.B.beta., can remove
NF-.kappa.B from functional preinitiation complexes in vitro transcription
experiments. Second, we showed that both I.kappa.Bs function in vivo not
only in the cytoplasm but also in the nucleus, where they inhibit
NF-.kappa.B binding to DNA. Third, the inhibitory activity of
I.kappa.B.beta., but not that of I.kappa.B.alpha., is facilitated by
phosphorylation of the C-terminal PEST sequence by ***casein*** kinase
II and/or by the interaction of NF-.kappa.B with high-mobility group
protein I (HMG I) on selected ***promoters*** . The unphosphorylated
form of I.kappa.B.beta. forms stable ternary complexes with NF-.kappa.B on
the DNA either in vitro or in vivo. These experiments suggest that
I.kappa.B.alpha. works as a postinduction repressor of NF-.kappa.B
independently of HMG I, whereas I.kappa.B.beta. functions preferentially
in ***promoters*** regulated by the NF-.kappa.B/HMG I complexes.

L25 ANSWER 3 OF 13 MEDLINE DUPLICATE 1
AN 96355620 MEDLINE
DN 96355620
TI Stat6 and JakI are common elements in platelet-derived growth factor and
interleukin-4 signal transduction pathways in NIH 3T3 fibroblasts.
AU Patel B K; Wang L M; Lee C C; Taylor W G; Pierce J H; LaRochelle W J
CS Laboratory of Cellular and Molecular Biology, National Cancer Institute,
Bethesda, Maryland 20892, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Sep 6) 271 (36) 22175-82.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199612
AB Both platelet-derived growth factor (PDGF) and interleukin-4 (IL-4) play
major roles in cell proliferation, differentiation, chemotaxis, and other
functional responses. Here, we demonstrate that Stat6, previously shown to
be activated by only IL-4 and IL-3, becomes activated after PDGF
stimulation of NIH 3T3 fibroblasts. PDGF BB, and to a lesser extent PDGF
AA, rapidly induced DNA binding activity from NIH 3T3 cell lysates
utilizing the ***immunoglobulin*** heavy chain germ line epsilon

promoter (Iepsilon) that specifically binds to Stat6 in an electrophoretic mobility shift assay. DNA binding activity could be detected within 5 min and reached maximum levels at approximately 20 min in parental NIH 3T3 cells. An identical mobility shift and time course of PDGF-mediated Iepsilon binding activity was more pronounced in lysates of NIH 3T3 transfectants overexpressing human Stat6 (NIH 3T3-Stat6). The observed radiolabeled Iepsilon mobility shift was competed by unlabeled Iepsilon as well as by the beta- ***casein*** gene ***promoter*** but not by the interferon-alpha-stimulated response element or the interferon-gamma response region of the guanylate-binding protein gene. A Stat6-specific polyclonal antisera also supershifted the PDGF-induced Iepsilon mobility shift. After PDGF BB treatment, a 100-kDa tyrosine phosphorylated species was detected in anti-Stat6 immunoprecipitates. Cycloheximide had little effect on Stat6 tyrosine phosphorylation. In addition to Stat6, Stat5a, and Stat5b, PDGF BB also induced Jak1 tyrosine phosphorylation suggesting a potential pathway for Stat activation. Strikingly, the concurrent addition of IL-4 enhanced PDGF BB-induced Iepsilon binding activity, Jak1 tyrosine phosphorylation, and [3H]thymidine incorporation. These results provide evidence that Stat6 and Jak1 are common elements in PDGF and IL-4 signaling pathways and suggest that IL-4 could play a role in potentiating certain known PDGF-induced biological responses.

L25 ANSWER 4 OF 13 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96096378 EMBASE
DN 1996096378
TI Phosphorylation of I.kappa.B.alpha. in the C-terminal PEST domain by ***casein*** kinase II affects intrinsic protein stability.
AU Lin R.; Beauparlant P.; Makris C.; Meloche S.; Hiscott J.
CS Lady Davis Medical Research Inst., 3755 Cote Ste. Catherine,Montreal, Que. H3T 1E2, Canada
SO Molecular and Cellular Biology, (1996) 16/4 (1401-1409). ISSN: 0270-7306 CODEN: MCEBD4
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English

AB The NF-.kappa.B/Rel transcription factors participate in the activation of immune system regulatory genes and viral early genes including the human immunodeficiency virus type 1 long terminal repeat. NF-.kappa.B/Rel proteins are coupled to inhibitory molecules, collectively termed I.kappa.B, which are responsible for cytoplasmic retention of NF-.kappa.B. Cell activation leads to the phosphorylation and degradation of I.kappa.B.alpha., permitting NF-.kappa.B/Rel translocation to the nucleus and target gene activation. To further characterize the signaling events that contribute to I.kappa.B.alpha. phosphorylation, a kinase activity was isolated from Jurkat T cells that specifically interacted with I.kappa.B.alpha. in an affinity chromatography step and phosphorylated I.kappa.B.alpha. with high specificity in vitro. By using an in-gel kinase assay with recombinant I.kappa.B.alpha. as substrate, two forms of the kinase (43 and 38 kDa) were identified. Biochemical criteria and immunological cross-reactivity identified the kinase activity as the alpha catalytic subunit of ***casein*** kinase II (CKII). Deletion mutants of I.kappa.B.alpha. (.DELTA.1 to .DELTA.4) localized phosphorylation to the C-terminal PEST domain of I.kappa.B.alpha.. Point mutation of residues T-291, S-283, and T-299 dramatically reduced phosphorylation of I.kappa.B.alpha. by the kinase in vitro. NIH-3T3 cells that stably expressed wild-type I.kappa.B.alpha. (wtI.kappa.B), double-point-mutated I.kappa.B.alpha.(T291A, S283A), or triple-point- mutated I.kappa.B.alpha.(T291A, S283A, T299A) under the control of the tetracycline- responsive ***promoter*** were generated. Constitutive phosphorylation of the triple point mutant was eliminated in vivo, although tumor necrosis factor- inducible I.kappa.B.alpha. degradation was unaffected. In cell lines and in transiently transfected cells, mutation of the CKII sites in I.kappa.B.alpha. resulted in a protein with increased intrinsic stability. Together with results demonstrating a role for N-terminal sites in inducer-mediated phosphorylation and degradation of I.kappa.B.alpha., these studies indicate that CKII sites in the C-terminal PEST domain are important for constitutive phosphorylation and intrinsic stability of I.kappa.B.alpha..

L25 ANSWER 5 OF 13 CAPLUS COPYRIGHT 1999 ACS
AN 1996:609130 CAPLUS
DN 125:273244
TI IL-10 induces DNA binding activity of three STAT proteins (Stat1, Stat3, and Stat5) and their distinct combinatorial assembly in the ***promoters*** of selected genes
AU Wehinger, Jens; Gouilleux, Fabrice; Groner, Bernd; Finke, Juergen; Mertelsmann, Roland; Weber-Nordt, Renate Maria
CS University of Freiburg Medical Center, Department of Hematology and Oncology, Hugstetter Str. 55, Freiburg, 79106, Germany
SO FEBS Lett. (1996), 394(3), 365-370 CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
AB Interaction of IL-10 with its receptor leads to the activation of STAT transcription factors. Herein the authors report the IL-10 dependent simultaneous activation of 3 STAT transcription factors: Stat1, Stat3, and Stat5. Upon IL-10 treatment multiple Stat proteins become simultaneously activated, and bind to different ***promoters*** with equal kinetics but form distinct homo- and heterodimeric transcriptionally active complexes depending on the STAT-consensus elements of a selected gene ***promoter*** . Upon IL-10 treatment Stat1, 3, and 5 bind to the GRR of the Fc.gamma.RI gene, activated Stat1 and 3 bind to the SIE sequence of the c-fos ***promoter*** and transcriptionally active Stat5 assembles at the PRL-STAT consensus sequence of the .beta.- ***casein*** gene. Thus, functionally relevant STAT dimerization is influenced by the activated cytokine receptor as well as the specific STAT consensus sequence present in a specific gene ***promoter*** .

L25 ANSWER 6 OF 13 MEDLINE DUPLICATE 2
AN 96358438 MEDLINE
DN 96358438
TI Regulation of somatostatin gene transcription by cyclic adenosine monophosphate.
AU Montminy M; Brindle P; Arias J; Ferreri K; Armstrong R
CS Clayton Foundation Laboratories for Peptide Biology, Salk Institute, La Jolla, CA 92037, USA.
NC GM37828 (NIGMS)
SO METABOLISM: CLINICAL AND EXPERIMENTAL, (1996 Aug) 45 (8 Suppl 1) 4-7. Ref: 12 Journal code: MUM. ISSN: 0026-0495.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199702
EW 19970204
AB Cyclic adenosine monophosphate (cAMP) stimulates transcription of
somatostatin and other target genes with burst-attenuation kinetics. The
kinetics of protein kinase (PK-A)-dependent cAMP response element binding
protein (CREB) phosphorylation closely parallel the changes in
transcription of cAMP-responsive genes by run-on assay. Nuclear
translocation of PK-A, visualized by microinjection of fluorescently
labeled PK-A holoenzyme, appears to represent the rate-limiting step in
CREB phosphorylation and transcriptional activation. We and others have
recently characterized a CREB-binding protein (CBP), which specifically
recognizes sequences within the Ser133 phosphorylated form of CREB. CBP
does not regulate the DNA binding, dimerization, or nuclear targeting
properties of CREB, but binds selectively to the kinase-inducible 60 amino
acid trans-activation domain (KID) of CREB, critical for PK-A-inducible
transcription. We developed an antiserum directed against amino acid
634-648 within the CREB-binding domain of CBP. We detected a 265-kd
polypeptide by Western blot as predicted from the cDNA, which coincided
with the predominant phospho-CREB-binding activity in Hela nuclear
extracts by "Far Western" blot assay. An identical phospho-CREB-binding
activity was also found in NIH-3T3 cells. This phospho-CREB-binding
protein appeared to be specific for Ser133-phosphorylated CREB, because no
such band was detected with CREB labeled to the same specific activity at
a nonregulatory phosphoacceptor site (Ser156) by ***casein*** kinase
II (CKII). Following microinjection into nuclei of NIH-3T3 cells, a cAMP
response element (CRE)-lacZ reporter was markedly induced by treatment
with 8-Br cAMP plus isobutyl methyl xanthine (IBMX). Coinjection of CBP
antiserum with the CRE-lacZ plasmid inhibited cAMP-dependent activity in a
dose-dependent manner, but control ***immunoglobulin*** G (IgG) had no
effect on this response. We can now begin reconstituting PK-A-dependent
transcription in vitro, using well-characterized proteins such as CREB,
TAF 110, and CBP. The assembly of such factors on cAMP-regulated
promoters like somatostain may enable responsiveness to a variety
of hormonal stimuli that employ cAMP as their second messenger.

L25 ANSWER 7 OF 13 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 3
AN 95305660 EMBASE
DN 1995305660
TI Interleukin 4-inducible phosphorylation of HMG-I(Y) is inhibited by
rapamycin.
AU Wang D.-Z.; Ray P.; Boothby M.
CS Dept. of Microbiology/Immunology, Vanderbilt Univ. School of Medicine,Nashville, TN 37232-2363, United States
SO Journal of Biological Chemistry, (1995) 270/39 (22924-22932).
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB The non-histone chromosomal protein HMG-I(Y) participates in repression of
transcription directed by a ***promoter*** which confers interleukin 4
(IL-4)- inducible activation in transfected B cell lines. Metabolic
labeling, phosphoamino acid analyses, and in vitro phosphorylation studies
demonstrate that IL-4 induces serine phosphorylation of HMG-I(Y) in B
lymphocytes. Phosphopeptide mapping shows that the predominant site of
phosphorylation contains a ***casein*** kinase II consensus motif. The
immunosuppressive agent rapamycin has been shown preferentially to inhibit
IgE production by IL-4- treated human B cells. It is shown here that
rapamycin inhibits both activation of the human germ line .epsilon.
promoter by IL-4 and IL-4-inducible phosphorylation of HMG-I(Y).
These findings demonstrate a rapamycin-sensitive pathway that transduces
signals from the IL-4 receptor to nuclear factors that regulate inducible
transcription. The affinity of normal nuclear HMG- I(Y) for DNA is
increased by dephosphorylation in vitro, whereas in vitro kinase reactions
using ***casein*** kinase II decrease recombinant HMG-I(Y) binding to
DNA. These data further suggest a novel mechanism in which phosphorylation
triggered by IL-4 or other cytokines could regulate the effects of
HMG-I(Y) on gene transcription.

L25 ANSWER 8 OF 13 CAPLUS COPYRIGHT 1999 ACS
AN 1994:210040 CAPLUS
DN 120:210040
TI Manufacture of foreign proteins in cattle and their accumulation in milk
IN Deboer, Herman A.; Strijker, Rein; Heyneker, Herbert L.; Platenburg,
Gerard; Lee, Sang He; Pieper, Frank
PA Genpharm International, Inc., USA
SO PCT Int. Appl., 178 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9325567	A1	19931223	WO 1993-US5724	19930615
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9345373	A1	19940104	AU 1993-45373	19930615
EP 652889	A1	19950517	EP 1993-915365	19930615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08504562	T2	19960521	JP 1993-501794	19930615
US 5633076	A	19970527	US 1993-154019	19931116
US 5741957	A	19980421	US 1995-461333	19950605

PRAI US 1992-898956 19920615
US 1989-444745 19891201
US 1990-619131 19901127
US 1993-77788 19930615
WO 1993-US5724 19930615
US 1993-154019 19931116
AB Expression cassettes using regulatory regions functional in mammary
secretory cells are used to direct the synthesis of proteins in cattle
mammary glands with subsequent accumulation of the protein in milk.
Methods for prepg. transgenic cattle by transformation and implantation of
embryos are described. The transgene is methylated and introduced into
fertilized oocytes and the oocytes cultured to the pre-implantation embryo

stage. Cells are then removed from the pre-implantation embryos and the
DNA digested with a restriction endonuclease capable of cleaving the
methylated transgene but not the unmethylated form. The development of
expression vectors using the 5'- and 3'-flanking sequences of the cattle
.alpha.S1 ***casein*** gene was demonstrated and an expression
cassette for a human lactoferrin cDNA constructed. Transgenic calves
carrying the expression cassette were obtained and one showing normal
sperm and a lack of mosaicism was obtained.

L25 ANSWER 9 OF 13 MEDLINE DUPLICATE 4
AN 92260636 MEDLINE
DN 92260636
TI Receptor properties of two varicella-zoster virus glycoproteins, gpI and
gpIV, homologous to herpes simplex virus gE and gI.
AU Litwin V; Jackson W; Grose C
CS Department of Microbiology, University of Iowa College of Medicine, Iowa
City 52242..
NC AI22795 (NIAID)
SO JOURNAL OF VIROLOGY, (1992 Jun) 66 (6) 3643-51.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199208
AB The varicella-zoster virus (VZV) genome contains 70 reading frames (ORF),
5 of which encode the glycoproteins gpI, gpII, gpIII, gpIV, and gpV. ORF
67 and 68 lie adjacent to each other in the unique short region of the VZV
genome and code for gpIV and gpI, respectively. These two genes, which are
contained within the HindIII C fragment of the VZV genome, were subcloned
in the correct orientation downstream from the ***promoter*** regions
of the eukaryotic expression vectors pCMV5 and pBJ. After transfection, 5
to 20% of the Cos cells bound antibody specific for the given
glycoprotein. In this study, it was shown that only the cells transfected
with the gpI construct bound to the Fc fragment of human
immunoglobulin G. Neither the transfected gpIV gene product nor
the vector only bound to the Fc fragment. Thus, VZV gpI is confirmed to be
the VZV-encoded Fc-binding glycoprotein. Like the wild-type form of gpI
expressed in VZV-infected cells, gpI precipitated from transfected cells
contained both N-linked and O-linked glycans and was heavily sialated. In
addition, the transfected gpI gene product was phosphorylated both in cell
culture and in protein kinase assays by mammalian ***casein*** kinases
I and II. Extensive computer-assisted analyses of the VZV gpI sequence, as
well as those of alphaherpesviral homolog glycoproteins, disclosed
properties similar to those of other cell surface receptors; these
included (i) exocytoplasmic regions rich in cysteine residues, (ii)
membrane-proximal regions with potential O-linked glycosylation sites, and
(iii) cytoplasmic domains with consensus phosphorylation sites.

L25 ANSWER 10 OF 13 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1992:468244 BIOSIS
DN BR43:89594
TI THE TRANSCRIPTION FACTOR CF1 REGULATES THE C-MYC THE IGH AND THE BETA
CASEIN ***PROMOTERS*** .
AU MEIER V; SCHMITT-NEY M; GRONER B
CS FRIEDRICH MIESCHER INST., CH-4002, BASEL.
SO 24TH ANNUAL MEETING OF THE SWISS SOCIETIES FOR EXPERIMENTAL BIOLOGY
(USGEB/USSBE), BASEL, SWITZERLAND, MARCH 19-20, 1992. EXPERIENTIA (BASEL).
(1992) 48 (ABSTR), A51.
CODEN: EXPEAM. ISSN: 0014-4754.
DT Conference
FS BR; OLD
LA English

L25 ANSWER 11 OF 13 CAPLUS COPYRIGHT 1999 ACS
AN 1991:625431 CAPLUS
DN 115:225431
TI Production of heterologous polypeptides by recombinant cattle and
transgenic methods
IN Heyneker, Herbert L.; Deboer, Herman A.; Strijker, Rein; Plantenburg,
Gerard; Lee, Sang He
PA Genpharm International, Inc., USA
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9108216	A1	19910613	WO 1990-US6874	19901130
W: AU, BR, CA, FI, JP, KR, LK, MC, NO, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2075206	AA	19910602	CA 1990-2075206	19901130
AU 9169608	A1	19910626	AU 1991-69608	19901130
AU 656720	B2	19950216		
EP 502976	A1	19920916	EP 1991-901026	19901130
EP 502976	B1	19960703		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 140027	E	19960715	AT 1991-901026	19901130
EP 737746	A2	19961016	EP 1995-203326	19901130
EP 737746	A3	19961023		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2090299	T3	19961016	ES 1991-901026	19901130
RU 2095414	C1	19971110	RU 1990-5052392	19901130
CN 1053446	A	19910731	CN 1990-109733	19901201
NO 9202996	A	19920729	NO 1992-2996	19920729
FI 9203485	A	19920731	FI 1992-3485	19920731
US 5633076	A	19970527	US 1993-154019	19931116
US 5741957	A	19980421	US 1995-461333	19950605
PRAI US 1989-444745		19891201		
US 1990-619131		19901127		
EP 1991-901026		19901130		
WO 1990-US6874		19901130		
US 1992-898956		19920615		
US 1993-77788		19930615		
US 1993-154019		19931116		

AB A method for prepg. transgenic cows which secrete recombinant proteins
into their milk is described. The gene to be expressed in mammary tissue
is fused to a mammary tissue-specific ***promoter*** , e.g. that of the
casein gene, a signal sequence, and a 3' flanking sequence
functional in cattle. The chimeric gene is first methylated, e.g. by
cloning it in a prokaryotic host. Fertilized oocytes are then transformed
with this gene, and the fertilized oocytes are cultured to the
preimplantation embryo stage. A cell is removed from the embryo to test
for the presence of the desired gene: the chimeric methylated gene is
resistant to restriction endonuclease cleavage. The hemiembryo remaining
after removing the cell is cloned to prep. multiple embryos which are
implanted into a cow to produce transgenic offspring. The milk from the
transgenic cows can be used in food formulations, esp. infant formulas. A
chimeric gene comprising human lactoferrin cDNA flanked by bovine
.alpha.S1- ***casein*** ***promoter*** and signal sequence and 3'
regions was prepd. Transgenic cows secreting lactoferrin into their

milk
were produced using this gene according to the above procedure.

L25 ANSWER 12 OF 13 MEDLINE DUPLICATE 5
AN 92107650 MEDLINE
DN 92107650
TI Upstream box/TATA box order is the major determinant of the direction of
transcription.
AU Xu L C; Thali M; Schaffner W
CS Institut fur Molekularbiologie II, Universitat Zurich, Switzerland.
SO NUCLEIC ACIDS RESEARCH, (1991 Dec 25) 19 (24) 6699-704.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199204
AB Mammalian gene ***promoters*** for transcription by RNA polymerase II
are typically organized in the following order: upstream sequence
motif(s)/TATA box/initiation site. Here we report studies in which the
order, orientation and DNA sequences of these three elements are varied to
determine how these affect polarity of transcription. We have constructed
promoters with an 'octamer' upstream sequence ATTTGCAT (or its
complement ATGCAAAT) in combination with several different TATA boxes and
initiation (cap) sites, and tested these ***promoters*** in
transfection experiments with cultured cells. TATA boxes derived from the
adenovirus major late ***promoter*** (TATAAAA), ***immunoglobulin***
kappa light chain (TTATATA) and heavy chain (TAAATATA) ***promoter***
functioned equally well or even better when inverted. Only the beta-globin
TATA box (CATAAAA) was poorly active when inverted. In addition, a
symmetrical TATA box (TATATATA) derived from a ***casein*** gene was
very active. Our results suggest that the asymmetry of most TATA boxes
(consensus TATAAAA) is not a primary determinant of the polarity of
transcription. We also found that the initiation (cap) site, which usually
consists of an adenine embedded in a pyrimidine-rich region
(PyPyCAPyPyPyPyPy), was permissive towards sequence alterations; even a
randomly composed sequence worked well. However, an inverted, hence
purine-rich, cap site reduced transcript levels to 1/7th, as did an oligo
G sequence. Irrespective of the presence of a cap site, the configuration:
'TATA box/octamer' yielded a strong leftward, rather than rightward
transcription. From this, we conclude that the polarity of transcription
is primarily determined by the linear order of an upstream sequence
relative to a TATA box, rather than by the individual orientations of
either of these two elements.

L25 ANSWER 13 OF 13 CAPLUS COPYRIGHT 1999 ACS
AN 1989:451714 CAPLUS
DN 111:51714
TI Manufacture of recombinant proteins by secretion into milk of transgenic
mammals
IN Meade, Harry; Longberg, Nils
PA Biogen N. V., Neth.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 8810118	A1	19881229	WO 1988-US2134	19880623
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4873316	A	19891010	US 1987-65994	19870623
EP 347431	A1	19891227	EP 1988-906454	19880623
EP 347431	B1	19951004		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02500798	T2	19900322	JP 1988-505800	19880623
AT 128625	E	19951015	AT 1988-906454	19880623
US 5750172	A	19980512	US 1995-460959	19950605
PRAI US 1987-65994		19870623		
WO 1988-US2134		19880623		
US 1989-332293		19890331		
US 1993-109865		19930820		
US 1994-322984		19941014		

AB A method for producing desired proteins by producing transgenic mammals
which secrete the protein into the milk is described. A section of the
bovine .alpha. S-1 ***casein*** gene contg. the ***promoter*** and
signal sequence was cloned. This DNA sequence was ligated to tissue-type
plasminogen activator (tPA) cDNA via DNA contg. RNA processing splice
sites (which allow the ***casein*** signal sequence RNA to be spliced
to the tPA-encoding RNA) to prep. pCAS1151. Preimplantation fertilized
mice embryos were microinjected with this (linearized) DNA and then
implanted in pseudopregnant female mice. Of 262 embryos injected and
implanted, 23 live pups were born, 5 of which contained the desired DNA
sequences. Male G0 mice were bred with females. Females of the G1
progeny which contained the tPA sequence produced 0.2-0.5 .mu.g tPA/mL
milk.

=> s l8

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L26 652 L8

=> s l26 and promoter/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L27 0 L26 AND PROMOTER/AB,BI

=> s l26 and (construct# or vector# or transgen?)/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L28 0 L26 AND (CONSTRUCT# OR VECTOR# OR TRANSGEN?)/AB,BI

=> d his

(FILE 'HOME' ENTERED AT 16:55:03 ON 04 AUG 1999)

FILE 'MEDLINE' ENTERED AT 16:55:09 ON 04 AUG 1999
L1 4 S IMMUNOGLOBULIN AND WHEY ACIDIC PROTEIN/AB,BI
L2 4 S IMMUNOGLOBULIN# AND WHEY ACIDIC PROTEIN/AB,BI
L3 0 S IMMUNOGLOBULIN# AND BETA-LACTOGLOBULIN PROMOTER/AB,BI
L4 0 S IMMUNOGLOBULIN# AND CASEIN PROMOTER/AB,BI
L5 0 S IMMUNOGLOBULIN# AND BETA-CASEIN PROMOTER/AB,BI
L6 0 S IMMUNOGLOBULIN# AND KAPPA-CASEIN PROMOTER/AB,BI
L7 0 S IMMUNOGLOBULIN# AND LACTALBUMIN

```
PROMOTER/AB,BI
L8        96 S IMMUNOGLOBULIN# AND
LACTALBUMIN/AB,BI
L9         0 S L8 AND (CONSTRUCT# OR VECTOR#)/AB,BI
L10        0 S L8 AND TRANSGEN?/AB,BI
L11      190 S IMMUNOGLOBULIN# AND CASEIN/AB,BI
L12        8 S L11 AND (CONSTRUCT# OR VECTOR#)/AB,BI

   FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS'
ENTERED AT 17:05:15 ON 04
   AUG 1999
L13        13 S L1
L14         6 DUP REM L13 (7 DUPLICATES REMOVED)
L15        23 S L2
L16        10 S L2 NOT L1
L17        10 DUP REM L16 (0 DUPLICATES REMOVED)
L18         2 S L4
L19         2 DUP REM L18 (0 DUPLICATES REMOVED)
L20       909 S IMMUNOGLOBULIN# AND
BETA-LACTOGLOBULIN/AB,BI
L21         2 S L20 AND PROMOTER#/AB,BI
L22         2 DUP REM L21 (0 DUPLICATES REMOVED)
L23      1345 S L11
L24        24 S L23 AND PROMOTER#/AB,BI
L25        13 DUP REM L24 (11 DUPLICATES REMOVED)
L26       652 S L8
L27         0 S L26 AND PROMOTER/AB,BI
L28         0 S L26 AND (CONSTRUCT# OR VECTOR# OR
TRANSGEN?)/AB,BI

=> e meade harry/au

E1         2   MEADE H W/AU
E2         1   MEADE HARLAN DONNELLY/AU
E3        42 --> MEADE HARRY/AU
E4        28   MEADE HARRY M/AU
E5         2   MEADE HASH T J/AU
E6         2   MEADE HASH TARA J/AU
E7         2   MEADE HAZEL/AU
E8         5   MEADE HAZEL W/AU
E9         1   MEADE HAZEL WHITTIG/AU
E10        2   MEADE HOWARD M/AU
E11        3   MEADE HUERTA P/AU
E12        2   MEADE HUERTA PATRICIA/AU

=> s e3-e4

L29       70 ("MEADE HARRY"/AU OR "MEADE HARRY
M"/AU)

=> s l29 and immunoglobulin# and promoter#/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L30        2 L29 AND IMMUNOGLOBULIN# AND
PROMOTER#/AB,BI

=> dup rem l30

PROCESSING COMPLETED FOR L30
L31        2 DUP REM L30 (0 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS -
CONTINUE? Y/(N):y


L31 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN  1995:780439 CAPLUS
DN  123:190527
TI  Transgenic production of antibodies in milk and usefulness for
    diagnostics, therapy, or industry
IN  ***Meade, Harry*** ; Ditullio, Paul; Pollock, Daniel
PA  Genzyme Transgenics Corp., USA
SO  PCT Int. Appl., 24 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.      KIND  DATE         APPLICATION NO.
DATE
    --------------- ----  -------- ---------------- --------
PI  WO 9517085      A1  19950629     WO 1994-US14795
19941220
        W: AU, CA, JP, NZ
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE
    US 5827690      A   19981027     US 1993-170579  19931220
    CA 2178941      AA  19950629     CA 1994-2178941 19941220
    AU 9515172      A1  19950710     AU 1995-15172   19941220
    AU 688845       B2  19980319
    EP 741515       A1  19961113     EP 1995-906691  19941220
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,
NL, PT, SE
    JP 09506779     T2  19970708     JP 1994-517602  19941220
    US 5849992      A   19981215     US 1995-410887  19950327
    AU 9873079      A1  19980820     AU 1998-73079   19980619
PRAI US 1993-170579  19931220
    WO 1994-US14795  19941220
AB  A method for the prodn. of monoclonal antibodies in mammal's
milk, through
    the creation of transgenic animals that selectively express foreign
    antibody genes in mammary epithelial cells.

L31 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN  1989:451714 CAPLUS
DN  111:51714
TI  Manufacture of recombinant proteins by secretion into milk of
transgenic
    mammals
IN  ***Meade, Harry*** ; Longberg, Nils
PA  Biogen N. V., Neth.
SO  PCT Int. Appl., 20 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.      KIND  DATE         APPLICATION NO.
DATE
    --------------- ----  -------- ---------------- --------
PI  WO 8810118      A1  19881229     WO 1988-US2134
19880623
        W: JP
        RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE
    US 4873316      A   19891010     US 1987-65994   19870623
    EP 347431       A1  19891227     EP 1988-906454  19880623
    EP 347431       B1  19951004
        R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
    JP 02500798     T2  19900322     JP 1988-505800  19880623
    AT 128625       E   19951015     AT 1988-906454  19880623
    US 5750172      A   19980512     US 1995-460959  19950605
PRAI US 1987-65994  19870623
    WO 1988-US2134  19880623
    US 1989-332293  19890331
    US 1993-109865  19930820
    US 1994-322984  19941014
AB  A method for producing desired proteins by producing transgenic
mammals
    which secrete the protein into the milk is described. A section of
the
    bovine .alpha. S-1 casein gene contg. the ***promoter*** and
signal
    sequence was cloned. This DNA sequence was ligated to
tissue-type
    plasminogen activator (tPA) cDNA via DNA contg. RNA
processing splice
    sites (which allow the casein signal sequence RNA to be spliced to
the
    tPA-encoding RNA) to prep. pCAS1151. Preimplantation
fertilized mice
    embryos were microinjected with this (linearized) DNA and then
implanted
    in pseudopregnant female mice. Of 262 embryos injected and
implanted, 23
    live pups were born, 5 of which contained the desired DNA
sequences. Male
    G0 mice were bred with females. Females of the G1 progeny
which contained
    the tPA sequence produced 0.2-0.5 .mu.g tPA/mL milk.

=> d 2 kwic


L31 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1999 ACS
IN  ***Meade, Harry*** ; Longberg, Nils
AB  . . . which secrete the protein into the milk is described. A
section
    of the bovine .alpha. S-1 casein gene contg. the ***promoter***
```

and
signal sequence was cloned. This DNA sequence was ligated to tissue-type
plasminogen activator (tPA) cDNA via DNA contg. RNA. . .
IT Caseins, biological studies
RL: BIOL (Biological study)
(gene for, ***promoter*** and signal sequence of, secretion of
recombinant protein into milk of transgenic mammals in relation to)
IT ***Immunoglobulins***
RL: PROC (Process)
(manuf. of, with transgenic mammals, by secretion into milk)
IT Molecular cloning
(of chimeric casein ***promoter*** and signal sequence-plasminogen
activator gene, for expression in transgenic mice and sheep)
IT Gene and Genetic element
RL: BIOL (Biological study)
(chimeric, ***promoter*** and signal sequence of milk-specific
protein-contg., in secretion of recombinant protein into milk of
transgenic mammals)
IT Plasmid and Episome
(pCAS1151, chimeric casein ***promoter*** and signal
sequence-plasminogen activator gene on, expression in transgenic mice
and sheep of)

=> e ditullio paul/au

E1	1	DITULLIO NW/AU
E2	19	DITULLIO P/AU
E3	32	--> DITULLIO PAUL/AU
E4	1	DITULLIO R/AU
E5	1	DITULLIO R M/AU
E6	4	DITULLIO ROBERT J/AU
E7	1	DITULLIO S/AU
E8	3	DITULLIO S A/AU
E9	9	DITULLIO V/AU
E10	9	DITULLIO VENANZIO/AU
E11	1	DITULLIO VENENZIO/AU
E12	1	DITULLO NICHOLAS W/AU

=> s e2-e3

L32 51 ("DITULLIO P"/AU OR "DITULLIO PAUL"/AU)

=> s l32 and immunoglob? and promoter#/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L33 1 L32 AND IMMUNOGLOB? AND PROMOTER#/AB,BI

=> d bib ab

L33 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
AN 1995:780439 CAPLUS
DN 123:190527
TI Transgenic production of antibodies in milk and usefulness for diagnostics, therapy, or industry
IN Meade, Harry; ***Ditullio, Paul*** ; Pollock, Daniel
PA Genzyme Transgenics Corp., USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9517085	A1	19950629	WO 1994-US14795	19941220
W: AU, CA, JP, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5827690	A	19981027	US 1993-170579	19931220
CA 2178941	AA	19950629	CA 1994-2178941	19941220
AU 9515172	A1	19950710	AU 1995-15172	19941220
AU 688845	B2	19980319		
EP 741515	A1	19961113	EP 1995-906691	19941220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09506779	T2	19970708	JP 1994-517602	19941220
US 5849992	A	19981215	US 1995-410887	19950327
AU 9873079	A1	19980820	AU 1998-73079	19980619
PRAI US 1993-170579		19931220		
WO 1994-US14795		19941220		

AB A method for the prodn. of monoclonal antibodies in mammal's milk, through
the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

=> e pollock daniel/au

E1	4	POLLOCK D S/AU
E2	2	POLLOCK D W/AU
E3	16	--> POLLOCK DANIEL/AU
E4	11	POLLOCK DANIEL A/AU
E5	7	POLLOCK DANIEL D/AU
E6	12	POLLOCK DARREN A/AU
E7	1	POLLOCK DARREN R/AU
E8	1	POLLOCK DAVE/AU
E9	19	POLLOCK DAVID/AU
E10	3	POLLOCK DAVID A/AU
E11	1	POLLOCK DAVID ALEXANDER/AU
E12	5	POLLOCK DAVID B/AU

=> s e3-e5

L34 34 ("POLLOCK DANIEL"/AU OR "POLLOCK DANIEL A"/AU OR "POLLOCK DANIEL D"/AU)

=> s l34 and immunoglob? and promoter#/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L35 1 L34 AND IMMUNOGLOB? AND PROMOTER#/AB,BI

=> d

L35 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
AN 1995:780439 CAPLUS
DN 123:190527
TI Transgenic production of antibodies in milk and usefulness for diagnostics, therapy, or industry
IN Meade, Harry; Ditullio, Paul; ***Pollock, Daniel***
PA Genzyme Transgenics Corp., USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9517085	A1	19950629	WO 1994-US14795	19941220
W: AU, CA, JP, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5827690	A	19981027	US 1993-170579	19931220
CA 2178941	AA	19950629	CA 1994-2178941	19941220
AU 9515172	A1	19950710	AU 1995-15172	19941220
AU 688845	B2	19980319		
EP 741515	A1	19961113	EP 1995-906691	19941220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09506779	T2	19970708	JP 1994-517602	19941220
US 5849992	A	19981215	US 1995-410887	19950327
AU 9873079	A1	19980820	AU 1998-73079	19980619
PRAI US 1993-170579		19931220		
WO 1994-US14795		19941220		

=> d his

(FILE 'HOME' ENTERED AT 16:55:03 ON 04 AUG 1999)

FILE 'MEDLINE' ENTERED AT 16:55:09 ON 04 AUG 1999
L1 4 S IMMUNOGLOBULIN AND WHEY ACIDIC PROTEIN/AB,BI
L2 4 S IMMUNOGLOBULIN# AND WHEY ACIDIC PROTEIN/AB,BI
L3 0 S IMMUNOGLOBULIN# AND

BETA-LACTOGLOBULIN PROMOTER/AB,BI
L4 0 S IMMUNOGLOBULIN# AND CASEIN PROMOTER/AB,BI
L5 0 S IMMUNOGLOBULIN# AND BETA-CASEIN PROMOTER/AB,BI
L6 0 S IMMUNOGLOBULIN# AND KAPPA-CASEIN PROMOTER/AB,BI
L7 0 S IMMUNOGLOBULIN# AND LACTALBUMIN PROMOTER/AB,BI
L8 96 S IMMUNOGLOBULIN# AND LACTALBUMIN/AB,BI
L9 0 S L8 AND (CONSTRUCT# OR VECTOR#)/AB,BI
L10 0 S L8 AND TRANSGEN?/AB,BI
L11 190 S IMMUNOGLOBULIN# AND CASEIN/AB,BI
L12 8 S L11 AND (CONSTRUCT# OR VECTOR#)/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 17:05:15 ON 04 AUG 1999
L13 13 S L1
L14 6 DUP REM L13 (7 DUPLICATES REMOVED)
L15 23 S L2
L16 10 S L2 NOT L1
L17 10 DUP REM L16 (0 DUPLICATES REMOVED)
L18 2 S L4
L19 2 DUP REM L18 (0 DUPLICATES REMOVED)
L20 909 S IMMUNOGLOBULIN# AND BETA-LACTOGLOBULIN/AB,BI
L21 2 S L20 AND PROMOTER#/AB,BI
L22 2 DUP REM L21 (0 DUPLICATES REMOVED)
L23 1345 S L11
L24 24 S L23 AND PROMOTER#/AB,BI
L25 13 DUP REM L24 (11 DUPLICATES REMOVED)
L26 652 S L8
L27 0 S L26 AND PROMOTER/AB,BI
L28 0 S L26 AND (CONSTRUCT# OR VECTOR# OR TRANSGEN?)/AB,BI
E MEADE HARRY/AU
L29 70 S E3-E4
L30 2 S L29 AND IMMUNOGLOBULIN# AND PROMOTER#/AB,BI
L31 2 DUP REM L30 (0 DUPLICATES REMOVED)
E DITULLIO PAUL/AU
L32 51 S E2-E3
L33 1 S L32 AND IMMUNOGLOB? AND PROMOTER#/AB,BI
E POLLOCK DANIEL/AU
L34 34 S E3-E5
L35 1 S L34 AND IMMUNOGLOB? AND PROMOTER#/AB,BI

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	164.98	172.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.78	-11.78

STN INTERNATIONAL LOGOFF AT 17:15:07 ON 04 AUG 1999

FILE 'USPAT' ENTERED AT 14:09:49 ON 05 AUG 1999

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 ********************************
 *     U.S. PATENT TEXT FILE    *
 *                              *
 * THE WEEKLY PATENT TEXT AND IMAGE DATA IS
CURRENT      *
 * THROUGH AUGUST 3,1999              *
 *                              *
 *                              *
 ********************************
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=> s lactalbumin promoter

```
      1127 LACTALBUMIN
     27862 PROMOTER
L1        5 LACTALBUMIN PROMOTER
            (LACTALBUMIN(W)PROMOTER)
```

=> d 1- cit ab

1. 5,852,224, Dec. 22, 1998, .alpha.-lactalbumin gene constructs; Julian
David Cooper, et al., 800/7; 435/69.1, 71.1; 800/13, 15, 18 [IMAGE AVAILABLE]

US PAT NO: 5,852,224 [IMAGE AVAILABLE] L1: 1 of 5

ABSTRACT:
The present invention utilizes genetic engineering techniques to prepare
non-human transgenic mammals that express human .alpha.-lactalbumin in
their milk at a concentration of 2 mg/ml or greater. The invention also includes methods of preparing human .alpha.-lactalbumin in, for example,
mice and cows. Also taught are methods for preparing human .alpha.-lactalbumin in which from one to four of its natural phenylalanine residues have been substituted by another amino acid.

2. 5,849,992, Dec. 15, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/14, 7, 15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L1: 2 of 5

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

3. 5,827,690, Oct. 27, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/7; 530/867 [IMAGE AVAILABLE]

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L1: 3 of 5

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

4. 5,589,604, Dec. 31, 1996, Expression of human protein C in mammary
tissue of transgenic mammals; William N. Drohan, et al., 800/7; 435/69.6,
212; 800/14, 15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,589,604 [IMAGE AVAILABLE] L1: 4 of 5

ABSTRACT:
Recombinant protein C characterized by a high percentage of active protein can be obtained in the milk of transgenic mammals that incorporate DNAs according to the present invention. Transgenic mammals
of the present invention are produced by introducing into developing embryos DNA that encodes protein C, such that the DNA is stably incorporated in the DNA of germ line cells of the mature mammals and
inherited in normal, mendelian fashion.

5. 5,523,226, Jun. 4, 1996, Transgenic swine compositions and methods;
Matthew B. Wheeler, 435/325; 424/9.1; 435/7.23, 378 [IMAGE AVAILABLE]

US PAT NO: 5,523,226 [IMAGE AVAILABLE] L1: 5 of 5

ABSTRACT:
Transgenic swine, and compositions and methods for making and using same,
are provided. Central to the invention are porcine (Sus scrofa) embryonic
stem cell lines and methods for establishing them. Cells of such lines are transformed with exogenous genetic material of interest and then used
to provide chimeric swine, which have germ cells comprising the exogenous
genetic material. The chimeric swine are bred to provide transgenic swine. Transgenic swine of the invention can be used to provide human
proteins or peptide hormones or can be used as xenograft donors.

=> d 1 4 5 claims

'CLAIMS' IS NOT A VALID FORMAT FOR FILE 'USPAT'
ENTER DISPLAY FORMAT (CIT):clms

US PAT NO: 5,852,224 [IMAGE AVAILABLE] L1: 1 of 5

CLAIMS:

CLMS(1)

We claim:

1. A method of producing non-human animal milk containing at least 2
mg/ml of an .alpha.-lactalbumin selected from the group consisting of:
(i) human .alpha.-lactalbumin; and
(ii) modified human .alpha.-lactalbumin having from one to four of the
natural phenylalanine residues substituted by other amino acid residues;
said method comprising:
(1) producing milk in the mammary gland of an adult transgenic, non-human placental mammal whose somatic and germ cells include a
genetic construct comprising, in the 5' to 3' direction and operatively linked:
(a) at least 1.8 kb of 5'-flanking sequence from the human .alpha.-lactalbumin gene including the .alpha.-**lactalbumin** **promoter**;
(b) a DNA sequence encoding
(1) a secretion signal; and
(2) an .alpha.-lactalbumin selected from the group consisting of:
(i) human .alpha.-lactalbumin; and
(ii) modified human .alpha.-lactalbumin having from one to four of the natural phenylalanine residues substituted by other amino acid residues;
(c) at least about 3 kb of 3'-flanking sequence from the human .alpha.-lactalbumin gene;
wherein said construct is expressed in the mammary gland of said mammal
and .alpha.-lactalbumin is produced in the milk at a level of at least 2 mg/ml; and
(2) collecting the milk produced in step (1), wherein said milk contains
at least 2 mg/ml of said human .alpha.-lactalbumin or said modified human .alpha.-lactalbumin.

CLMS(2)

2. A method of producing an .alpha.-lactalbumin selected from the group
consisting of:
(i) human .alpha.-lactalbumin; and
(ii) modified human .alpha.-lactalbumin having from one to four of the
natural phenylalanine residues substituted by other amino acid residues;
said method comprising producing, by the method of claim 1, non-human
animal milk containing at least 2 mg/ml of said .alpha.-lactalbumin and
extracting said .alpha.-lactalbumin from said milk.

CLMS(3)

3. A transgenic non-human mammal whose somatic and germ cells contain a
transgene construct, said transgene construct comprising, in the 5' to 3' direction and operatively linked:
(a) at least about 1.8 kb of 5'-flanking sequence from the human .alpha.-**lactalbumin** **promoter**:
(b) a DNA sequence encoding
(1) a signal sequence; and
(2) a .alpha.-lactalbumin selected from the group consisting of:
(i) human .alpha.-lactalbumin; and
(ii) a modified human .alpha.-lactalbumin having from one to four of the natural phenylalanine residues substituted by other amino acid residues;
(c) at least about 3 kb of 3'-flanking sequence from the human .alpha.-lactalbumin gene;
wherein said transgene construct is integrated into the genome of said mammal in such a way that said DNA sequence is expressed in the mammary
gland of said mammal to produce .alpha.-lactalbumin in the milk of said
mammal at a level of at least 2 mg/ml.

CLMS(4)

4. The transgenic non-human mammal of claim 3 wherein said mammal is a
mouse.

CLMS(5)

5. The transgenic non-human mammal of claim 3 wherein said mammal is a
cow.

US PAT NO: 5,589,604 [IMAGE AVAILABLE] L1: 4 of 5

CLAIMS:

CLMS(1)

What we claim is:

1. A transgenic non-human mammal that contains and expresses a human
protein C DNA construct in the cells of its mammary gland, wherein the
DNA construct consists of:
(a) a mammary gland promoter,
(b) a nucleotide sequence that encodes a signal peptide, wherein said signal peptide is effective in directing the secretion of an associated polypeptide into the milk of said transgenic non-human mammal, and wherein said signal peptide-encoding nucleotide sequence is operatively
associated with said mammary gland promoter, and
(c) a nucleotide sequence encoding human protein C that is operatively
associated with said signal peptide-encoding nucleotide sequence,
wherein human protein C is secreted into the milk of said transgenic non-human mammal, and when purified, said protein C has a specific activity more than about 80% of the specific activity of human protein
C isolated from human plasma, as determined by an assay of protein C
serine protease activity or anticoagulant activity, and
wherein said non-human mammal is selected from the group consisting of
mouse, pig, sheep, goat and cattle.

CLMS(2)

2. The transgenic non-human mammal of claim 1, wherein said promoter is
selected from the group consisting of a whey acidic protein promoter, a casein promoter, a **lactalbumin** **promoter** and a .beta.-lactoglobulin promoter.

CLMS(3)

3. The transgenic non-human mammal of claim 2, wherein promoter is a
whey acidic protein promoter or a .beta.-lactoglobulin promoter.

CLMS(4)

4. The transgenic non-human mammal of claim 3, wherein said promoter is
a whey acidic protein promoter.

CLMS(5)

5. The transgenic non-human mammal of claim 1, wherein said human protein C isolated from said transgenic non-human mammal has a specific
activity that is about 80% to about 100% of the specific activity of human protein C isolated from human plasma.

CLMS(6)

6. The transgenic non-human mammal of claim 5, wherein said specific
activity is determined by an activated partial thromboplastin clotting time assay.

CLMS(7)

7. The transgenic non-human mammal of claim 5, wherein said promoter is
a whey acidic protein promoter or a .beta.-lactoglobulin promoter.

CLMS(8)

8. A process for the production of protein C, comprising the steps of:
(a) providing a transgenic non-human mammal that contains and expresses
a human protein C DNA construct in the cells of its mammary gland, wherein the DNA construct consists of:
(i) a mammary gland promoter,
(ii) a nucleotide sequence that encodes a signal peptide, wherein said signal peptide is effective in directing the secretion of an associated polypeptide into the milk of said transgenic non-human mammal, and wherein said signal peptide-encoding nucleotide sequence
is operatively associated with said mammary gland promoter, and
(iii) a nucleotide sequence encoding human protein C that is operatively associated with said signal peptide-encoding nucleotide sequence,
wherein human protein C is secreted into the milk of said transgenic non-human mammal, and when purified, said protein C has a specific activity more than about 80% of the specific activity of human protein
C isolated from human plasma, as determined by an assay of protein C
serine protease activity or anticoagulant activity, and
wherein said non-human mammal is selected from the group consisting of
mouse, pig, sheep, goat and cattle,
(b) producing milk from said transgenic non-human mammal,
(c) collecting said milk, and
(d) isolating said protein C from said milk.

CLMS(9)

9. The process of claim 8, wherein said promoter is selected from the group consisting of a whey acidic protein promoter, a casein promoter, a
lactalbumin **promoter** and a .beta.-lactoglobulin promoter.

CLMS(10)

10. The process of claim 9, wherein promoter is a whey acidic protein promoter or a .beta.-lactoglobulin promoter.

CLMS(11)

11. The process of claim 10, wherein said promoter is a whey acidic protein promoter.

CLMS(12)

12. The transgenic non-human mammal of claim 8, wherein said human
protein C isolated from said transgenic non-human mammal has a specific
activity that is about 80% to about 100% of the specific activity of human protein C isolated from human plasma.

CLMS(13)

13. The transgenic non-human mammal of claim 12, wherein said specific

activity is determined by an activated partial thromboplastin clotting time assay.

CLMS(14)

14. The transgenic non-human mammal of claim 13, wherein said promoter
is a whey acidic protein promoter or a .beta.-lactoglobulin promoter.

CLMS(15)

15. A transgenic non-human mammal that contains and expresses a human
protein C DNA construct in the cells of its mammary gland, wherein the
DNA construct consists of:
(a) a mammary gland promoter selected from the group consisting of a whey acidic protein promoter, a casein promoter, a **lactalbumin** **promoter** and a .beta.-lactoglobulin promoter,
(b) a nucleotide sequence that encodes a signal peptide, wherein said signal peptide is effective in directing the secretion of an associated polypeptide into the milk of said transgenic non-human mammal, and wherein said signal peptide-encoding nucleotide sequence is operatively
associated with said mammary gland promoter, and
(c) a nucleotide sequence encoding human protein C that is operatively
associated with said signal peptide-encoding nucleotide sequence,
wherein human protein C is secreted into the milk of said transgenic non-human mammal, and when purified, said protein C has a specific activity more than about 80% of the specific activity of human protein
C isolated from human plasma, as determined by an assay of protein C
serine protease activity or anticoagulant activity, and
wherein said non-human mammal is selected from the group consisting of
mouse, pig, sheep, goat and cattle.

CLMS(16)

16. The transgenic non-human mammal of claim 15, wherein said human
protein C isolated from said transgenic non-human mammal has a specific
activity that is about 80% to about 100% of the specific activity of human protein C isolated from human plasma.

CLMS(17)

17. The transgenic non-human mammal of claim 16, wherein said specific
activity is determined by an activated partial thromboplastin clotting time assay.

CLMS(18)

18. A process for the production of protein C, comprising the steps of:
(a) providing a transgenic non-human mammal that contains and expresses
a human protein C DNA construct in the cells of its mammary gland, wherein the DNA construct consists of:
(i) a mammary gland promoter selected from the group consisting of a whey acidic protein promoter, a casein promoter, a **lactalbumin** **promoter** and a .beta.-lactoglobulin promoter,
(ii) a nucleotide sequence that encodes a signal peptide, wherein said signal peptide is effective in directing the secretion of an associated polypeptide into the milk of said transgenic non-human mammal, and wherein said signal peptide-encoding nucleotide sequence
is operatively associated with said mammary gland promoter, and
(iii) a nucleotide sequence encoding human protein C that is operatively associated with said signal peptide-encoding nucleotide sequence,
wherein human protein C is secreted into the milk of said transgenic non-human mammal, and when purified, said protein C has a specific activity more than about 80% of the specific activity of human protein
C isolated from human plasma, as determined by an assay of protein C
serine protease activity or anticoagulant activity, and
wherein said non-human mammal is selected from the group consisting of
mouse, pig, sheep, goat and cattle,
(b) producing milk from said transgenic non-human mammal,
(c) collecting said milk, and
(d) isolating said protein C from said milk.

CLMS(19)

19. The transgenic non-human mammal of claim 18, wherein said human
protein C isolated from said transgenic non-human mammal has a specific
activity that is about 80% to about 100% of the specific activity of human protein C isolated from human plasma.

CLMS(20)

20. The transgenic non-human mammal of claim 19, wherein said specific
activity is determined by an activated partial thromboplastin clotting time assay.

US PAT NO: 5,523,226 [IMAGE AVAILABLE] L1: 5 of 5

CLAIMS:

CLMS(1)

What is claimed is:

1. A method of obtaining an embryonic stem cell for incorporation into a swine embryo to form a chimeric swine, said method comprising:
(a) introducing a cell from a culture made by:
(i) culturing dissociated cells from a swine embryo in conditioned stem
cell medium in the presence or absence of a feeder layer, and
(ii) subculturing the culture until a stable culture with morphological features and growth parameters characteristic of an embryonic stem cell culture is established, into a SCID mouse;
(b) allowing a tumor to form in the mouse from the cell; and
(c) obtaining an embryonic stem cell from a culture that is shown to be
capable of producing a tumor in step b.

CLMS(2)

2. The method of claim 1, wherein the embryonic stem cell is characterized by an undifferentiated morphology indistinguishable from
the morphology of a cell from the culture of step a of claim 1 from which
a cell formed a tumor in step b of claim 1.

CLMS(3)

3. A method for determining the cell types in which a genetic complement
is expressed, said method comprising:
(a) introducing a swine embryonic stem cell Which comprises the genetic
complement into an immunocompromised mouse to produce a tumor;
(b) placing the tumor in suitable conditions to allow the tumor to differentiate into a plurality of recognizable cell types and to empress the genetic complement;
(c) excising the tumor; and
(d) analyzing the differentiated cell types to determine in which cell types the genetic complement is expressed.

CLMS(4)

4. An embryonic stem cell obtained from a culture that is capable of forming a tumor in a SCIDS mouse in accordance with the method of claim
1.

CLMS(5)

5. A culture initiated from an embryonic stem cell of claim 4.

=> d 4 kwic

US PAT NO: 5,589,604 [IMAGE AVAILABLE] L1: 4 of 5

CLAIMS:

CLMS(2)

2. . . . 1, wherein said promoter is selected from the group consisting of a whey acidic protein promoter, a casein promoter, a **lactalbumin** **promoter** and a .beta.-lactoglobulin promoter.

CLAIMS:

CLMS(9)

9. . . . 8, wherein said promoter is selected from the group consisting of a whey acidic protein promoter, a casein promoter, a **lactalbumin** **promoter** and a .beta.-lactoglobulin promoter.

CLAIMS:

CLMS(15)

15. . . .
(a) a mammary gland promoter selected from the group consisting of a whey acidic protein promoter, a casein promoter, a **lactalbumin** **promoter** and a .beta.-lactoglobulin promoter,
(b) a nucleotide sequence that encodes a signal peptide, wherein said signal peptide is effective in directing. . .

CLAIMS:

CLMS(18)

18. . . .
(i) a mammary gland promoter selected from the group consisting of a
whey acidic protein promoter, a casein promoter, a **lactalbumin** **promoter** and a .beta.-lactoglobulin promoter,
(ii) a nucleotide sequence that encodes a signal peptide, wherein said signal peptide is effective in directing. . .

=> d 4 fro

US PAT NO: 5,589,604 [IMAGE AVAILABLE] L1: 4 of 5
DATE ISSUED: Dec. 31, 1996
TITLE: Expression of human protein C in mammary tissue of transgenic mammals
INVENTOR: William N. Drohan, Springfield, VA
Tracy D. Wilkins, Blacksburg, VA
William H. Velander, Blacksburg, VA
John L. Johnson, Blacksburg, VA
ASSIGNEE: American Red Cross, Washington, DC (U.S. corp.)
Virginia Intellectual Property Division, Blacksburg, VA (U.S. corp.)
APPL-NO: 08/247,484
DATE FILED: May 23, 1994
REL-US-DATA: Continuation of Ser. No. 638,995, Jan. 11, 1991, abandoned.
INT-CL: [6] C12N 5/00; C12N 15/00; C12N 9/48; C12P 21/04
US-CL-ISSUED: 800/2; 435/69.6, 212
US-CL-CURRENT: 800/7; 435/69.6, 212; 800/14, 15, 16, 17, 18
SEARCH-FLD: 800/2; 435/172.3
REF-CITED:

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4,873,316	10/1989	Meade et al.
4,992,373	2/1991	Bang et al.

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WO88/00239	1/1988	World Intellectual Property Organization
WO88/01648	3/1988	World Intellectual Property Organization
WO90/05188	5/1990	World Intellectual Property Organization

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ART-UNIT: 184
PRIM-EXMR: Deborah Crouch
LEGAL-REP: Foley & Lardner

ABSTRACT:
Recombinant protein C characterized by a high percentage of active protein can be obtained in the milk of transgenic mammals that incorporate DNAs according to the present invention. Transgenic mammals
of the present invention are produced by introducing into developing embryos DNA that encodes protein C, such that the DNA is stably incorporated in the DNA of germ line cells of the mature mammals and
inherited in normal, mendelian fashion.

20 Claims, 5 Drawing Figures

=> d 3 fro

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L1: 3 of 5
DATE ISSUED: Oct. 27, 1998
TITLE: Transgenic production of antibodies in milk
INVENTOR: Harry Meade, Newton, MA
Paul DiTullio, Framingham, MA
Daniel Pollock, Medway, MA
ASSIGNEE: Genzyme Transgenics Corporatiion, Framingham, MA (U.S. corp.)
APPL-NO: 08/170,579
DATE FILED: Dec. 20, 1993
INT-CL: [6] C12P 21/04; C12N 15/00
US-CL-ISSUED: 435/69.6, 172.3; 530/867; 800/2, DIG.1; 935/60
US-CL-CURRENT: 800/7; 530/867
SEARCH-FLD: 435/172.3, 69.1, 69.6; 530/867; 536/24.1; 800/2, DIG.1; 935/60
REF-CITED:

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4,873,316	10/1989	Meade et al.	530/412
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M-A Persuy et al (1992) European J Biochemistry 205: 887-893.
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NM Greenberg et al (1991) Proc Natl Acad Sci USA 88: 8327-8331.
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LM Houdebine (1994) J Biotechnol 34:269-287.
ART-UNIT: 184
PRIM-EXMR: Bruce R. Campell
LEGAL-REP: Lahive & Cockfield, LLP

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.
13 Claims, 4 Drawing Figures

=> d l fro

US PAT NO: 5,852,224 [IMAGE AVAILABLE] L1: 1 of 5
DATE ISSUED: Dec. 22, 1998
TITLE: .alpha.-lactalbumin gene constructs
INVENTOR: Julian David Cooper, Blacksburg, VA
Angelika Elisabeth Schnieke, Edinburgh, United Kingdom
ASSIGNEE: PPL Therapeutics (Scotland) Limited, Edinburgh, United
Kingdom (foreign corp.)
APPL-NO: 08/381,691
DATE FILED: Jan. 31, 1995
FRN-PRIOR: United Kingdom 9425326 Dec. 15, 1994
INT-CL: [6] C12N 15/09; C12N 15/11; C12N 15/12; C12P 21/00
US-CL-ISSUED: 800/2; 435/69.1, 71.1, 172.3; 935/34, 52, 70
US-CL-CURRENT: 800/7; 435/69.1, 71.1; 800/13, 15, 18
SEARCH-FLD: 800/2; 536/23.1, 24.1; 435/320.1, 240.2, 177.3, 69.1,
71.1; 350/365; 935/34, 52, 70
REF-CITED:

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Transgenic Rats", Molecular Reproduction And Development 33: 160-164
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a new molecular form of human alpha-lactalbumin" pp. 425-429 (1992).
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its rat counterpart", pp. 609-620 (1987).
ART-UNIT: 162
PRIM-EXMR: Brian R. Stanton
LEGAL-REP: Seidel, Gonda, Lavorgna & Monaco, PC

ABSTRACT:
The present invention utilizes genetic engineering techniques to prepare
non-human transgenic mammals that express human .alpha.-lactalbumin in
their milk at a concentration of 2 mg/ml or greater. The invention also includes methods of preparing human .alpha.-lactalbumin in, for example,
mice and cows. Also taught are methods for preparing human .alpha.-lactalbumin in which from one to four of its natural phenylalanine residues have been substituted by another amino acid.
5 Claims, 24 Drawing Figures

=> d his

(FILE 'USPAT' ENTERED AT 14:09:49 ON 05 AUG 1999)
L1 5 S LACTALBUMIN PROMOTER

=> log y

U.S. Patent & Trademark Office LOGOFF AT 14:15:04 ON 05 AUG 1999

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.14	-2.14

STN INTERNATIONAL LOGOFF AT 14:15:17 ON 05 AUG 1999

Connection closed by remote host

requirements are also taken into account, then Tyr3/9-Tyr31-Tyr53-Tyr80 is
preferred. Two DNA constructs, pHA-1 (contg. the human .alpha.-lactalbumin gene and flanking regions) and pOBHA (contg. the human
.alpha.-lactalbumin gene driven by the ovine .beta.-lactoglobulin promoter), were injected into mouse embryos to give rise to ***transgenic*** animals, expressing up to .apprx.3 mg/mL milk. The
bovine .alpha.-lactalbumin gene was also cloned and expressed in mice.
PCR primer oligonucleotides were designed for site-specific mutagenesis of
specific phenylalanine codons based on protein modeling, nutritional
aspects, and on amino acid variants present in either native .alpha.-lactalbumin or lysozyme genes from different species. The addn.
of extra poly(Arg) or Arg/Lys residues at the C-terminus of the .alpha.-lactalbumin assisted purifn. of endogenous protein. Improved
expression of mutagenized bovine .alpha.-lactalbumin was achieved by
control with the human .alpha.- ***lactalbumin*** ***promoter*** .

L3 ANSWER 7 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1993:227545 CAPLUS
DN 118:227545
TI Bovine alpha-lactalbumin gene promoter and its use in protein manufacture
with ***transgenic*** female mammals
IN Bleck, Gregory T.; Bremel, Robert D.
PA Wisconsin Milk Marketing Board, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9304165	A1	19930304	WO 1992-US6549	19920806
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
CA 2093659	AA	19930214	CA 1992-2093659	19920806
AU 9224119	A1	19930316	AU 1992-24119	19920806
AU 663101	B2	19950928		
EP 555435	A1	19930818	EP 1992-916978	19920806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
JP 06502550	T2	19940324	JP 1993-504341	19920806
US 5530177	A	19960625	US 1993-71601	19930604
US 5850000	A	19981215	US 1996-621100	19960322

PRAI US 1991-744765 19910813
WO 1992-US6549 19920806
US 1993-71601 19930604
AB A variant of the bovine .alpha.- ***lactalbumin*** ***promoter*** which correlates with good milk prodn. is claimed.
Transgenic
female mice contg. the bovine .alpha.-lactalbumin gene contg. this variation produced high levels of .alpha.-lactalbumin (>1 mg/mL) in their
milk. Three other potentially significant variations in the steroid response element and RNA polymerase binding region were noted.

L3 ANSWER 8 OF 10 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 91246508 EMBASE
DN 1991246508
TI Erratum: The bovine .alpha.- ***lactalbumin*** ***promoter*** directs expression of ovine trophoblast interferon in the mammary gland of
transgenic mice (FEBS Letters (1991) Vol. 284 (19-22)).
AU Stinnakre M.G.; Volotte J.L.; Soulier S.; L'Haridon R.; Charlier M.; Gaye
P.; Mercier J.C.
CS Laboratoire de Genetique Biochimique, I.N.R.A., 78350 Jouy-en-Josas,
France
SO FEBS Letters, (1991) 288/1-2 (247).
ISSN: 0014-5793 CODEN: FEBLAL
CY Netherlands
DT Journal; Errata
FS 029 Clinical Biochemistry
LA English

L3 ANSWER 9 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1991:672494 CAPLUS
DN 115:272494
TI The bovine .alpha.- ***lactalbumin*** ***promoter*** directs
expression of ovine trophoblast interferon in the mammary gland of ***transgenic*** mice [Erratum to document cited in CA115(7):66096k]
AU Stinnakre, M. G.; Vilotte, J. L.; Soulier, S.; L'Haridon, R.; Charlier,
M.; Gaye, P.; Mercier, J. C.
CS Lab. Physiol. Comp., Univ. Paris VI, Paris, 75005, Fr.
SO FEBS Lett. (1991), 288(1-2), 247
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
AB Errors in the author addresses have been cor. The errors were not reflected in the abstr. or the index entries.

L3 ANSWER 10 OF 10 MEDLINE DUPLICATE 3
AN 91285097 MEDLINE
DN 91285097
TI The bovine alpha- ***lactalbumin*** ***promoter*** directs
expression of ovine trophoblast interferon in the mammary gland of ***transgenic*** mice [published erratum appears in FEBS Lett 1991 Aug
19;288(1-2):247].
AU Stinnakre M G; Vilotte J L; Soulier S; L'Haridon R; Charlier M; Gaye P;
Mercier J C
CS Laboratoire de Physiologie Comparee, Universite Paris VI, France..
SO FEBS LETTERS, (1991 Jun 17) 284 (1) 19-22.
Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199110
AB A hybrid construct derived from ovine trophoblastin cDNA and bovine
alpha-lactalbumin-encoding gene, was injected into the pronuclei of mouse
eggs. In one of the resulting ***transgenic*** mouse lines, expression
of the hybrid construct was detected and found to be limited to the mammary gland of lactating females which secreted active ovine trophoblastin. This strongly suggests that important cis-acting DNA sequences involved in tissue-specific expression of the bovine gene are
located within the second half of the 3' untranslated region, or/and the
proximal 5' and 3' regions flanking the transcriptional unit.

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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	SESSION	TOTAL
FULL ESTIMATED COST		25.37	25.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

substrate for endogenous amidating activity in the mammary gland. Full
characterization of the released sCT demonstrated it to be equivalent to
synthetic standard in terms of structure, purity, and potency.

L3 ANSWER 4 OF 10 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:532816 BIOSIS
DN PREV199800532816
TI Production of ***transgenic*** pigs and mice containing the gene
encoding human insulin-like growth factor I (IGF-I) under control of the
bovine alpha- ***lactalbumin*** ***promoter*** and regulatory
regions.
AU Bleck, G. T. (1); Monaco, M. H.; Donovan, S. M.; Wheeler, M. B. (1)
CS (1) Dep. Animal Sci., Univ. Ill., Urbana, IL USA
SO Journal of Dairy Science, (1998) Vol. 81, No. SUPPL. 1, pp. 213.
Meeting Info.: Joint Meeting of the American Dairy Science Association and
the American Society of Animal Science Denver, Colorado, USA July 28-31,
1998 Amercian Society of Animal Science
. ISSN: 0022-0302.
DT Conference
LA English

L3 ANSWER 5 OF 10 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 2
AN 1996:186466 BIOSIS
DN PREV199698742595
TI Genetic modification of bovine beta-casein and its expression in the milk
of ***transgenic*** mice.
AU Choi, Byung-Kwon; Bleck, Gregory T.; Wheeler, Matthew B.; Jimenez-Flores,
Rafael (1)
CS (1) Dep. Dairy Sci., California Polytechnic State Univ., San Luis Obispo,
CA 93407 USA
SO Journal of Agricultural and Food Chemistry, (1996) Vol. 44, No. 3, pp.
953-960.
ISSN: 0021-8561.
DT Article
LA English
AB Genomic vectors containing mutant bovine beta-casein with putative
glycosylation sites were constructed to study the functional properties of
glycosylated beta-casein and its possible effects in milk. The mutation
was performed by PCR-based site-directed mutagenesis. The tripeptide
sequence, Asn-X-Ser, was generated between Asn-68 and Asn-73 in mature
beta-casein. The resulting beta-casein mutants were designated pCJB68 and
pCJB6873. pCJB68 carries a substitution of Ser-70 for Leu-70 (Asn-68-Ser-69-Ser-70-Pro-7l), and pCJB6873 carries a substitution of
Ser-70-Ser-71 for Leu-70-Pro-71 (Asn-68-Ser-69-Ser-70-Ser-7l). The two
mutated genomic constructs were placed under control of the bovine alpha-
lactalbumin ***promoter*** , and lines of mice expressing the
pCJB68 and pCJB6873 have been established. The milk from ***transgenic*** mice contained bovine beta-casein at levels up to 2-3
mg/mL. N-Linked glycosylation of bovine beta-casein in the pCJB6873 line
was confirmed by peptide-N-glycosidase F treatment, but glycosylation of
bovine beta-casein did not occur in pCJB68 mice. In addition, mouse casein
micelles containing glycosylated bovine beta-casein showed the largest
median diameter and rough outer surface, compared to normal mouse casein
micelles and micelles from ***transgenic*** milk containing bovine
beta-casein.

L3 ANSWER 6 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1995:511593 CAPLUS
DN 122:257982
TI Modified .alpha.-lactalbumins containing few or no phenylalanines for
dietary supplementation in hyperphenylalaninemia
IN Colman, Alan; Wright, Gordon; Sawyer, Lindsay; Rigden, Daniel John
PA Pharmaceutical Proteins Ltd., UK
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9502692	A1	19950126	WO 1994-GB1514	19940713

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2167155	AA	19950126	CA 1994-2167155	19940713
AU 9471306	A1	19950213	AU 1994-71306	19940713
AU 698597	B2	19981105		
EP 711344	A1	19960515	EP 1994-920557	19940713

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

CN 1127528	A	19960724	CN 1994-192790	19940713
JP 09500273	T2	19970114	JP 1994-504407	19940713
ZA 9405217	A	19960115	ZA 1994-5217	19940715
WO 9602640	A1	19960201	WO 1995-GB1651	19950712

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2193513	AA	19960201	CA 1995-2193513	19950712
AU 9528962	A1	19960216	AU 1995-28962	19950712
AU 700224	B2	19981224		
EP 765390	A1	19970402	EP 1995-924467	19950712

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

CN 1157635	A	19970820	CN 1995-194129	19950712
JP 10502816	T2	19980317	JP 1995-504802	19950712
ZA 9505850	A	19960219	ZA 1995-5850	19950713

PRAI GB 1993-14802 19930716
WO 1994-GB1514 19940713
GB 1994-25326 19941215
US 1995-381691 19950131
GB 1995-3822 19950225
WO 1995-GB1651 19950712
AB Modified .alpha.-lactalbumin, e.g. of bovine or human origin, comprising
fewer phenylalanine residues than wild-type .alpha.-lactalbumin may be
used as a dietary component for suffers of hyperphenylalaninemia.
Preferably, all of the phenylalanine residues are replaced. The modified
.alpha.-lactalbumin may be expressed in the mammary gland of non-human
host animals so as to accumulate in, and if desired be sepd. from, their
milk. Thus, residues Phe-9 (or Phe-3 in human), Phe-31, Phe-53, and
Phe-80 in bovine .alpha.-lactalbumin are substituted with Tyr, Leu, Met,
Trp, Ile, Ser, or Arg. If selection of the substituting amino acid is
made solely on the basis of energy minimization and structural
considerations, then Tyr3/9-Leu31-Tyr53-Tyr80 is preferred; if nutritional

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**********STN Columbus **********
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FILE 'HOME' ENTERED AT 14:12:22 ON 05 AUG 1999

=> file medline embase biosis inpadoc caplus

COST IN U.S. DOLLARS                SINCE FILE    TOTAL
                                    ENTRY SESSION
FULL ESTIMATED COST                      0.15     0.15

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FILE 'EMBASE' ENTERED AT 14:12:34 ON 05 AUG 1999
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COPYRIGHT (C) 1999 European Patent Office, Vienna (EPO)

FILE 'CAPLUS' ENTERED AT 14:12:34 ON 05 AUG 1999
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=> s lactalbumin promoter/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L1        23 LACTALBUMIN PROMOTER/AB,BI

=> s l1 and transgen?/ab,bi

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L2        17 L1 AND TRANSGEN?/AB,BI

=> dup rem l2

PROCESSING COMPLETED FOR L2
L3        10 DUP REM L2 (7 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 10 ANSWERS -
CONTINUE? Y/(N):y


L3  ANSWER 1 OF 10  MEDLINE                  DUPLICATE 1
AN  1999159717    MEDLINE
DN  99159717
TI  Production of low-lactose milk by ectopic expression of intestinal
    lactase
    in the mouse mammary gland [see comments].
CM  Comment in: Nat Biotechnol 1999 Feb;17(2):135-6
AU  Jost B; Vilotte J L; Duluc I; Rodeau J L; Freund J N
CS  Institut National de la Sante et de la Recherche Medicale, Unite
    381,
    Strasbourg, France.
SO  NATURE BIOTECHNOLOGY, (1999 Feb) 17 (2) 160-4.
    Journal code: CQ3. ISSN: 1087-0156.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Priority Journals
EM  199906
EW  19990603
AB  We have investigated, in mice, an in vivo method for producing
    low-lactose
    milk, based on the creation of ***transgenic*** animals carrying
    a
    hybrid gene in which the intestinal lactase-phlorizin hydrolase
    cDNA was
    placed under the control of the mammary-specific alpha-
    ***lactalbumin***
    ***promoter*** . ***Transgenic*** females expressed
    lactase protein
    and activity during lactation at the apical side of mammary alveolar
    cells. Active lactase was also secreted into milk, anchored in the
    outer
    membrane of fat globules. Lactase synthesis in the mammary gland
    caused a
    significant decrease in milk lactose (50-85%) without obvious
    changes in
    fat and protein concentrations. Sucklings nourished with
    low-lactose milk
    developed normally. Hence, these data validate the use of
    ***transgenic*** animals expressing lactase in the mammary
    gland to
    produce low-lactose milk in vivo, and they demonstrate that the
    secretion
    of an intestinal digestive enzyme into milk can selectively modify
    its
    composition.

L3  ANSWER 2 OF 10  CAPLUS  COPYRIGHT 1999 ACS
AN  1999:482480  CAPLUS
TI  Introduction of a proximal stat5 site in the murine .alpha.-
    ***lactalbumin***  ***promoter***  induces prolactin
    dependency in
    vitro and improves expression frequency in vivo
AU  Soulier, Solange; Lepourry, Laurence; Stinnakre, Marie-Georges;
    Langley,
    Brett; L'Huillier, Phil J.; Paly, Jacqueline; Djiane, Jean; Mercier,
    Jean-Claude; Vilotte, Jean-Luc
CS  Laboratoire de GCnktique Biochimique et de Cytogknetique,
    INRA,
    Jouv-en-Josas, 78352, Fr.
SO  Transgenic Res. (1999), 8(1), 23-31
    CODEN: TRSEES; ISSN: 0962-8819
PB  Kluwer Academic Publishers
DT  Journal
LA  English
AB  In order to establish a possible correlation between in vitro
    prolactin
    induction and the transcriptional activity of mammary gene
    promoters in
    ***transgenic*** mice, a functional Stat5-binding site was
    created by
    means of site-directed mutagenesis at position -70 on a 560 bp
    murine
    .alpha.-lactalbumin promotor linked to a CAT reporter gene.
    Surprisingly,
    the wild-type promoter was constitutively active in vitro and could
    not be
    induced by prolactin. Introducing the proximal Stat5 site abolished
    this
    constitutive activity and resulted in prolactin dependence in both
    CHO-KI-
    and HCl 1-transfected cells. In ***transgenic*** mice, both the
    frequency of lines expressing the ***transgene*** and the
    prevalence
    of mid to late pregnancy expression were increased.

L3  ANSWER 3 OF 10  BIOSIS  COPYRIGHT 1999 BIOSIS
AN  1998:479280  BIOSIS
DN  PREV199800479280
TI  Production of biologically active salmon calcitonin in the milk of
    ***transgenic*** rabbits.
AU  McKee, Colin (1); Gibson, Allan; Dalrymple, Mike; Emslie,
    Liz; Garner,
    Ian; Cottingham, Ian
CS  (1) PPL Therapeutics Ltd., Roslin, Edinburgh EH25 9PP UK
SO  Nature Biotechnology, (July, 1998) Vol. 16, No. 7, pp. 647-651.
    ISSN: 1087-0156.
DT  Article
LA  English
AB  Salmon calcitonin (sCT) is an example of one of the many
    bioactive
    peptides that require amidation of the carboxy terminus for full
    potency.
    We describe a method for the production of amidated sCT in the
    mammary
    gland of ***transgenic*** rabbits. Expression of a fusion
    protein
    comprising human alpha lactalbumin joined by an enterokinase
    cleavable
    linker to sCT was directed to the mammary gland under the control
    of the
    ovine beta lactoglobulin promoter. C-terminal amidation in vivo
    was
    achieved by extending the sCT by a single glycine residue that
    provides a
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production of detectable levels of 2'-fucosyl-lactose in the milk of said mammal.

CLMS(2)

2. The mammal according to claim 1, wherein said mammal is selected from
the group consisting of a mouse, a rabbit, a pig, a goat, a sheep and a cow.

=> e meade, harry

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	MEADD/BI
E2	USPAT	306	MEADE/BI
E3	USPAT	0 -->	MEADE, HARRY/BI
E4	USPAT	1	MEADELSON/BI
E5	USPAT	6	MEADEN/BI
E6	USPAT	20	MEADER/BI
E7	USPAT	3	MEADERING/BI
E8	USPAT	3	MEADERS/BI
E9	USPAT	1	MEADEVILLE/BI
E10	USPAT	1	MEADHATCHER/BI
E11	USPAT	2	MEADI/BI
E12	USPAT	4	MEADIA/BI

=> e meade, harry/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	2	MEADE, EDWIN M/IN
E2	USPAT	1	MEADE, GEORGE E/IN
E3	USPAT	5 -->	MEADE, HARRY/IN
E4	USPAT	3	MEADE, HARRY M/IN
E5	USPAT	1	MEADE, HAZEL/IN
E6	USPAT	3	MEADE, HAZEL W/IN
E7	USPAT	3	MEADE, JAMES H/IN
E8	USPAT	1	MEADE, JAMES M/IN
E9	USPAT	1	MEADE, JAMES P/IN
E10	USPAT	3	MEADE, JAMES R/IN
E11	USPAT	1	MEADE, JEFFREY/IN
E12	USPAT	5	MEADE, JOHN/IN

=> s e3-e4

5 "MEADE, HARRY"/IN
3 "MEADE, HARRY M"/IN
L15 8 ("MEADE, HARRY"/IN OR "MEADE, HARRY M"/IN)

=> d l- fro

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L15: 1 of 8
DATE ISSUED: Dec. 15, 1998

TITLE: Transgenic production of antibodies in milk
INVENTOR: **Harry Meade**, Newton, MA
Paul Ditullio, Framingham, MA
Daniel Pollock, Medway, MA
ASSIGNEE: Genzyme Transgenics Corporation, Framingham, MA (U.S. corp.)
APPL-NO: 08/410,887
DATE FILED: Mar. 27, 1995
REL-US-DATA: Division of Ser. No. 170,579, Dec. 20, 1993.
INT-CL: [6] C12N 5/00; C12N 15/00
US-CL-ISSUED: 800/2, DIG.1
US-CL-CURRENT: 800/14, 7, 15, 16, 17, 18
SEARCH-FLD: 800/2, DIG.1; 435/172.3
REF-CITED:

U.S. PATENT DOCUMENTS

4,816,397	3/1989	Boss et al.	425/68
4,816,567	3/1989	Cabily et al.	530/387
4,873,316	10/1989	Meade et al.	530/412
5,322,775	6/1994	Clark et al.	435/69.1

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WO 90/04036	10/1989	World Intellectual Property Organization21/8
WO 90/04036	4/1990	World Intellectual Property Organization
WO 92/03918	8/1991	World Intellectual Property Organization
WO 93/12227	12/1992	World Intellectual Property Organization

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MA Persuy et al (1992) European J Biochem 205:887-893.
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Clark, A., Simons, P. Wilmut, I., Lathe, R. (1987) Bio/Technology 5:20/24.
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Clark, A., Bessos, H., Bishop, J., Brown, P., Harriis, S., Lathe, R., McClenaghan, M., Prowse, C., Simons, J., Whitelaw, C., Wilmut, I., (1989) Bio/Technology 7:487-492.
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Buhler, Th. A., Bruyere, Th., Went, D., Stranzinger, G., Buiki, K., (1990) Bio/Technology 8:140-143.
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Clark, A.J. et al., "Pharmaceuticals From Transgenic Livestock" Trends in Biotechnology, 5(1): 20-24 (1987).
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Dec 20th 1993 1997

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ART-UNIT: 162
PRIM-EXMR: Bruce R. Campbell
LEGAL-REP: Lahive & Cockfield, LLP

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

10 Claims, 4 Drawing Figures

US PAT NO: 5,843,705 [IMAGE AVAILABLE] L15: 2 of 8
DATE ISSUED: Dec. 1, 1998
TITLE: Transgenically produced antithrombin III
INVENTOR: Paul DiTullio, Framingham, MA
Harry Meade, Newton, MA
Edward S. Cole, Mendon, MA
ASSIGNEE: Genzyme Transgenic Corporation, Framingham, MA (U.S. corp.)
APPL-NO: 08/391,743
DATE FILED: Feb. 21, 1995
INT-CL: [6] C12P 21/06; C12N 9/48
US-CL-ISSUED: 435/69.1; 530/393, 392, 386, 380, 360, 412, 832; 514/8, 21; 435/320.1, 172.3, 172.1, 325; 800/2; 424/152.1, 535; 930/240
US-CL-CURRENT: 800/7; 424/157.1, 535; 435/212, 320.1, 325; 514/8, 21; 530/360, 380, 386, 392, 393, 412, 832; 930/240
SEARCH-FLD: 435/320.1, 172.3, 240.2, 69.1, 325, 212, 172.1; 530/412, 360, 393, 70, 386, 832, 380; 514/8, 21; 800/2; 424/157.1, 535
REF-CITED:

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4,517,294	5/1985	Bock et al.	435/69.4
4,632,981	12/1986	Bock et al.	514/8
4,873,316	10/1989	Meade et al.	530/412
5,366,894	11/1994	Clarke et al.	435/320.1

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Edmundo et al J. of Cellular Biochemistry Supplement O(180) 1994 p. 265.
Wall Theriogenology 45:57-68 (1996).

ART-UNIT: 163
PRIM-EXMR: Christopher S.F. Low
LEGAL-REP: Louis Myers

ABSTRACT:
This invention relates to transgenically produced human Antithrombin III (tgATIII). The human ATIII produced by the transgenic process of the present invention has a monosaccharide composition which comprises N-acetylgalactosamine (GalNAc) along with fucose, N-acetylglucosamine, galactose, mannose, and N-acetylneuraminic acid/N-glycolyneuraminic acid. The monosaccharide composition differs with that of plasma derived ATIII (phATIII). It has been found that tgATIII has an increased clearance rate when compared to phATIII.

13 Claims, 11 Drawing Figures

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L15: 3 of 8
DATE ISSUED: Oct. 27, 1998
TITLE: Transgenic production of antibodies in milk
INVENTOR: **Harry Meade**, Newton, MA
Paul DiTullio, Framingham, MA
Daniel Pollock, Medway, MA
ASSIGNEE: Genzyme Transgenics Corporatiion, Framingham, MA (U.S. corp.)
APPL-NO: 08/170,579
DATE FILED: Dec. 20, 1993
INT-CL: [6] C12P 21/04; C12N 15/00
US-CL-ISSUED: 435/69.6, 172.3; 530/867; 800/2, DIG.1; 935/60
US-CL-CURRENT: 800/7; 530/867
SEARCH-FLD: 435/172.3, 69.1, 69.6; 530/867; 536/24.1; 800/2, DIG.1; 935/60
REF-CITED:

U.S. PATENT DOCUMENTS

4,816,397	3/1989	Boss et al.	435/68
4,816,567	3/1989	Cabilly et al.	530/387
4,873,316	10/1989	Meade et al.	530/412
5,322,775	6/1994	Clark et al.	435/69.1

FOREIGN PATENT DOCUMENTS

WO 90/04036	10/1989	World Intellectual Property Organization21/8
WO 92/03918	8/1991	World Intellectual Property Organization
WO 93/12227	12/1992	World Intellectual Property Organization

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Clark, A., Bessos, H., Bishop, J., Brown, P., Harris, S., Lathe, R., McClenaghan, M., Prowse, C., Simons, J., Whitelaw, C., Wilmut, L., (1989) Bio/Technology 7:487-492.
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ART-UNIT: 184
PRIM-EXMR: Bruce R. Campell
LEGAL-REP: Lahive & Cockfield, LLP

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.
13 Claims, 4 Drawing Figures

US PAT NO: 5,750,172 [IMAGE AVAILABLE] L15: 4 of 8
DATE ISSUED: May 12, 1998
TITLE: Transgenic non human mammal milk
INVENTOR: **Harry Meade**, Newton, MA
Nils Lonberg, New York, NY
ASSIGNEE: Pharming B.V., Leiden, Netherlands (foreign corp.)
APPL-NO: 08/460,959
DATE FILED: Jun. 5, 1995
REL-US-DATA: Continuation of Ser. No. 322,984, Oct. 14, 1994, which is
a continuation of Ser. No. 109,865, Aug. 20, 1993, abandoned, which is a continuation of Ser. No. 332,293, Mar. 31, 1989, abandoned, which is a division of Ser. No. 65,994, Jun. 23, 1987, Pat. No. 4,873,316.
INT-CL: [6] C12P 21/06; C12P 21/02; C12P 21/04
US-CL-ISSUED: 426/580; 435/69.1, 69.4, 69.51, 69.52, 69.6, 183, 215;
800/2, DIG.1
US-CL-CURRENT: 426/580; 435/69.1, 69.4, 69.51, 69.52, 69.6, 183, 215;
800/7
SEARCH-FLD: 800/2, DIG.1, 3, 4; 435/172.1, 69.1, 69.4, 69.51, 69.52,
69.6, 215, 183; 935/63, 9, 11, 13, 14, 53; 530/832, 833; 426/580
REF-CITED:

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ART-UNIT: 189
PRIM-EXMR: Deborah Crouch
LEGAL-REP: Townsend & Townsend & Crew LLP

ABSTRACT:
This invention relates to the production of recombinant proteins, such as coagulation factors VIII and IX, tissue plasminogen activator (TPA), urokinase, growth hormone, insulin, interferons, interleukins, peptide hormones and immunoglobulins, in mammals' milk. Particularly, this invention relates to an expression system which when transgenically incorporated into a mammal permits the female species of that mammal to produce the desired recombinant protein in or along with its milk. This invention also relates to the transgenic mammal that produces the desired recombinant product in its milk.
5 Claims, No Drawings

US PAT NO: 5,688,677 [IMAGE AVAILABLE] L15: 5 of 8
DATE ISSUED: Nov. 18, 1997
TITLE: Deoxyribonucleic acids containing inactivated hormone responsive elements
INVENTOR: Karl M. Ebert, Millbury, MA
Paul DiTullio, Framingham, MA
Seng Hing Cheng, Wellesley, MA
Harry M. Meade, Newton, MA
Alan Edward Smith, Dover, MA
ASSIGNEE: Genzyme Corporation, Framingham, MA (U.S. corp.)
APPL-NO: 08/135,809
DATE FILED: Oct. 13, 1993
INT-CL: [6] C12N 15/06; C12N 15/12
US-CL-ISSUED: 435/240.1; 536/24.1, 23.5
US-CL-CURRENT: 536/23.5, 24.1
SEARCH-FLD: 536/23.5, 24.1; 514/44; 435/6, 172.3, 240.1, 69.1; 800/2
REF-CITED:

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Van Brunt, Bio/Technology 6: 1150 (1988).
ART-UNIT: 184
PRIM-EXMR: James Martinell

ABSTRACT:
A DNA comprising at least one inactivated hormone responsive element and
a nucleic acid sequence encoding a membrane-associated protein is described. Therapeutic compositions and cells including the DNA are also
described. Other aspects of the invention include methods of treating subjects having cystic fibrosis which include administering an effective amount of the DNA to subjects having cystic fibrosis such that functional
cystic fibrosis transmembrane conductance regulator is produced by the
subject at a level which is not detrimental to the subject. The present invention also pertains to a method of introducing the DNA into a cell such that the membrane-associated protein is produced at a level which is
not detrimental to the cell and cells produced by this method. Still other aspects of the invention include a method of assaying DNA for the
presence or absence of a hormone responsive element in a species in which
the hormone responsive element is functional and a method of selectively
breeding female transgenic mammals which produce a protein of interest.

11 Claims, 14 Drawing Figures

US PAT NO: 5,272,254 [IMAGE AVAILABLE] L15: 6 of 8
DATE ISSUED: Dec. 21, 1993
TITLE: Production of streptavidin-like polypeptides
INVENTOR: **Harry M. Meade**, Newton, MA
Jeffrey L. Garwin, Bedford, MA
ASSIGNEE: Biogen Inc., Cambridge, MA (U.S. corp.)
APPL-NO: 07/800,158
DATE FILED: Nov. 27, 1991
REL-US-DATA: Division of Ser. No. 185,329, Apr. 21, 1988, Pat. No.
5,168,049, which is a continuation of Ser. No. 656,873, Oct. 2, 1984, abandoned.
INT-CL: [5] C07K 13/00; C07K 7/00
US-CL-ISSUED: 530/350, 300, 825
US-CL-CURRENT: 530/350, 300, 825
SEARCH-FLD: 530/350, 825, 300
REF-CITED:

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4,411,994	10/1983	Gilbert et al.	435/69.7
4,839,293	6/1989	Cantor et al.	

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ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Gabriele E. Bugaisky
LEGAL-REP: James F. Haley, Denise L. Loring

ABSTRACT:
DNA sequences, hybrid DNA sequences, recombinant DNA molecules and processes for producing streptavidin-like polypeptides and for producing fused proteins consisting of a streptavidin-like polypeptide joined end to end with another protein, polypeptide, peptide or amino acid. The DNA sequences, hybrid DNA sequences and recombinant DNA molecules of this invention are characterized in that they include DNA fragments that code for streptavidin-like polypeptides. These DNA sequences, hybrid DNA sequences and recombinant DNA molecules and the hosts transformed with them may be employed in the processes of this invention to produce streptavidin-like polypeptides and fused proteins.
5 Claims, 7 Drawing Figures

US PAT NO: 5,168,049 [IMAGE AVAILABLE] L15: 7 of 8
DATE ISSUED: Dec. 1, 1992
TITLE: Production of streptavidin-like polypeptides
INVENTOR: **Harry M. Meade**, Newton, MA
Jeffrey L. Garwin, Bedford, MA
ASSIGNEE: Biogen, Inc., Cambridge, MA (U.S. corp.)
APPL-NO: 07/185,329
DATE FILED: Apr. 21, 1988
REL-US-DATA: Continuation of Ser. No. 656,873, Oct. 2, 1984, abandoned.
INT-CL: [5] C12N 15/00; C12N 15/03; C12N 15/04; C12N 15/05; C12N 15/06; C12N 15/11; C12N 15/31; C12N 15/70; C12P 21/00; C12P 21/02
US-CL-ISSUED: 435/69.1, 69.7, 69.8, 172.3, 240.1, 240.2, 240.4, 252.3, 252.33, 252.35, 255, 256, 320.1; 536/27; 935/10, 11
US-CL-CURRENT: 435/69.1, 69.7, 69.8, 252.3, 252.33, 252.35, 254.11, 254.2, 320.1, 366
SEARCH-FLD: 435/68, 70, 71, 91, 172.1, 172.3, 252.3, 252.31-252.35, 255, 256, 320, 69.1, 71.2, 320.1; 514/2; 536/27; 935/10, 11, 22, 29, 33, 38, 39, 47, 48, 66-75
REF-CITED:

U.S. PATENT DOCUMENTS

4,338,397	7/1982	Gilbert et al.	435/68
4,411,994	10/1983	Gilbert et al.	435/71
4,839,293	6/1989	Cantor et al.	435/320

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Maniatis et al., "Construction of Genomic Libraries In Cosmid Vectors", Molecular Cloning, A Laboratory Manual, pp. 295-305 (Maniatis, Fritch and Sambrook, ed., 1982).
Edlund et al, "Isolation of cDNA sequences coding for a part of human tissue plasminogen activator", Proc. Natl. Acad. Sci. USA 80: 349 (1983).
Hoffmann et al, "Iminobiotin affinity columns and their application to retrieval of streptavidin", Proc. Natl Acad. Sci. USA 77: 4666 (1980).
Roberts et al, "A general method for maximizing the expression of a cloned gene", Proc. Natl. Acad. Sci. USA 76: 760 (1979).
Hitzeman et al, "Expression of a human gene for interferon in yeast", Nature 293: 717 (1981).
ART-UNIT: 185
PRIM-EXMR: James Martinell
LEGAL-REP: James F. Haley, Jr., Denise L. Loring

ABSTRACT:
DNA sequences, hybrid DNA sequences, recombinant DNA molecules and processes for producing streptavidin-like polypeptides and for producing fused proteins consisting of a streptavidin-like polypeptide joined end to end with another protein, polypeptide, peptide or amino acid. The DNA sequences, hybrid DNA sequences and recombinant DNA molecules of this invention are characterized in that they include DNA fragments that code for streptavidin-like polypeptides. These DNA sequences, hybrid DNA sequences and recombinant DNA molecules and the hosts transformed with them may be employed in the processes of this invention to produce streptavidin-like polypeptides and fused proteins.
35 Claims, 7 Drawing Figures

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L15: 8 of 8
DATE ISSUED: Oct. 10, 1989
TITLE: Isolation of exogenous recombinant proteins from the milk of transgenic mammals
INVENTOR: **Harry Meade**, Newton, MA
Nils Lonberg, New York, NY
ASSIGNEE: Biogen, Inc., Cambridge, MA (U.S. corp.)
APPL-NO: 07/065,994
DATE FILED: Jun. 23, 1987
INT-CL: [4] C07K 3/02; C07K 3/12; C07K 3/18; C12N 15/00
US-CL-ISSUED: 530/412, 360, 361, 833, 832, 416, 417, 418; 435/68, 172.1, 172.3, 240.2; 935/53, 55, 70, 111; 800/1; 536/27, 28, 29
US-CL-CURRENT: 800/7; 435/69.1, 69.2, 69.4, 69.5, 69.6, 69.8; 530/360, 361, 416, 417, 418, 832, 833; 536/23.1, 23.4, 23.5; 800/18
SEARCH-FLD: 435/68, 172.1, 172.3, 226, 240.2; 530/832, 833, 412, 360, 361, 303; 800/1; 935/53, 55, 70; 536/27, 28, 29
REF-CITED:

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4,376,072	3/1983	Connolly	530/382
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0264166	4/1988	European Patent Office	
WO88/00239	1/1988	World Intellectual Property Organization	
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1299-303, May 1987).
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Brinster et al., Cell, 27, 223-31, Nov. 1981.

ART-UNIT: 186
PRIM-EXMR: Margaret Moskowitz
ASST-EXMR: Jeff P. Kushan
LEGAL-REP: James F. Haley, Jr., Teresa L. Solomon

ABSTRACT:
This invention relates to the production of recombinant proteins in mammals' milk. Particularly, this invention relates to an expression system comprising the mammal's casein promoter which when transgenically
incorporated into a mammal permits the female species of that mammal to
produce the desired recombinant protein in or along with its milk. This invention also relates to the transgenic mammal that produces the desired
recombinant product in its milk.

3 Claims, 1 Drawing Figures

=> d 1- clms

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L15: 1 of 8

CLAIMS:

CLMS(1)

What is claimed is:

1. A transgenic non-human mammal all of whose germ cells and somatic
cells contain a heterologous immunoglobulin protein-coding sequence operatively linked to a promoter sequence that directs the preferential expression of said protein-coding sequence in mammary gland epithelial
cells, thereby providing a heterologous and assembled immunoglobulin in
the milk of said mammal wherein said heterologous and assembled immunoglobulin is in a functional configuration and is produced at levels
of at least about 1 mg/ml in the milk of said mammal.

CLMS(2)

2. The transgenic mammal of claim 1 wherein said immunoglobulin comprises a tetrameric antibody directed against a pathogen.

CLMS(3)

3. The transgenic mammal of claim 1 wherein said immunoglobulin comprises a tetrameric antibody directed against a biologically active peptide.

CLMS(4)

4. The transgenic mammal of claim 1 wherein said biologically active peptide is selected from the group consisting of erythropoietin, tissue plasminogen activator and gamma interferon.

CLMS(5)

5. The transgenic mammal of claim 1 wherein said immunoglobulin comprises a tetrameric antibody directed against an enzyme.

CLMS(6)

6. The transgenic mammal of claim 1 wherein said mammal is selected from
the group consisting of mice, cows, sheep, goats, and pigs.

CLMS(7)

7. The transgenic mammal of claim 1 wherein said promoter is selected
from the group consisting of the casein promoter, the beta lactoglobulin
promoter, the whey acid protein promoter, and the lactalbumin promoter.

CLMS(8)

8. The transgenic mammal of claim 1 wherein said immunoglobulin comprises heavy and light chains.

CLMS(9)

9. The transgenic mammal of claim 1 wherein said immunoglobulin is of
human origin.

CLMS(10)

10. A transgenic non-human goat all of whose germ cells and somatic cells contain a heterologous immunoglobulin protein-coding sequence operatively linked to a promoter sequence that directs the preferential expression of said protein-coding sequence in mammary gland epithelial
cells, thereby providing a heterologous and assembled immunoglobulin in
the milk of said goat, wherein said heterologous and assembled immunoglobulin is in a functional configuration and is produced at levels
of at least about 1 mg/ml in the milk of said goat.

US PAT NO: 5,843,705 [IMAGE AVAILABLE] L15: 2 of 8

CLAIMS:

CLMS(1)

The invention claimed is:

1. A method for producing human antithrombin III in goat milk, comprising:
a. producing a transgenic goat that expresses in mammary tissue a transgene which encodes a human antithrombin III, wherein the human
antithrombin III is secreted into the milk produced by the transgenic goat;
b. collecting milk from the transgenic goat which milk contains the human antithrombin III; and
c. isolating the human antithrombin III from the collected milk, wherein
the human antithrombin III isolated from milk has faster clearance time
and an increased affinity for heparin both compared to human antithrombin III isolated from human plasma.

CLMS(2)

2. A glycosylated human antithrombin III, wherein a glycosylated human
antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a
transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is
secreted into the milk produced by the transgenic goat; and
wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising GalNac;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(3)

3. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising Fuc, GaINAc, GlcNAC, Gal, Man, and NANA/NGNA;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(4)

4. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising oligomannose and/or hybrid oligosaccharide structures;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(5)

5. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising primarily an oligomannose or hybrid type structure on one site and complex oligosaccharide on the remaining 3 sites,
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(6)

6. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) a monosaccharide composition which is partially sialylated;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(7)

7. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) a monosaccharide composition comprising sialic acid which includes NGNA;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(8)

8. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising a fucose on its proximal GlcNAc on each of the sites having oligosaccharides;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(9)

9. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising N-acerylglucosamine and mannose;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(10)

10. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is secreted into the milk produced by the transgenic goat; and wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising N-acetylglucosamine, galactose and mannose;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(11)

11. A glycosylated human antithrombin III, wherein a glycosylated human antithrombin III is made by the method of isolating the glycosylated human antithrombin III from milk, wherein the milk is collected from a

transgenic goat, which goat expresses in mammary tissue a transgene encoding human antithrombin III and wherein the human antithrombin III is
secreted into the milk produced by the transgenic goat; and
wherein the glycosylated human antithrombin III has the following properties:
a) monosaccharide glycosylation comprising N-acetylglucosamine, N-acetylgalactosamine and mannose;
b) no O-linked glycosylation;
c) faster plasma clearance time and an increased affinity for heparin both compared to human antithrombin III that is isolated from human plasma.

CLMS(12)

12. The glycosylated human antithrombin III of any one of claim 2, 3, 4,
5, 6, 7, 8, 9, 10 or 11, wherein the plasma clearance time of the transgenically produced antithrombin III is at least about 10 times faster than the plasma clearance time of the naturally occurring plasma antithrombin III.

CLMS(13)

13. The glycosylated human antithrombin III of any one of claim 2, 3, 4,
5, 6, 7, 8, 9, 10 or 11, wherein the affinity for heparin of the transgenically produced antithrombin III results in at least about 1000 fold enhanced affinity for thrombin as compared to the naturally occurring plasma antithrombin III.

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L15: 3 of 8

CLAIMS:

CLMS(1)

What is claimed is:

1. A high level expression method for providing a heterologous and assembled immunoglobulin, in the milk of a transgenic mammal comprising:
obtaining milk from a transgenic mammal having introduced into its germline a heterologous immunoglobulin protein-coding sequence operatively linked to a promoter sequence that results in the preferential expression of said protein-coding sequence in mammary gland epithelial cells, thereby providing said heterologous and assembled immunoglobulin in the milk of said mammal, wherein said
heterologous and assembled immunoglobulin is a functional configuration
and is produced at level of at least about 1 mg/ml in the milk of said mammal.

CLMS(2)

2. The method of claim 1 wherein said mammal is selected from the group
consisting of mice, sheep, and pigs.

CLMS(3)

3. The method of claim 1 wherein said promoter is selected from the group consisting of the beta lactoglobulin promoter, whey acid protein promoter, and the lactalbumin promoter.

CLMS(4)

4. The method of claim 1 wherein said immunoglobulin comprises heavy and
light chains.

CLMS(5)

5. The method of claim 1 wherein said immunoglobulin is of human origin.

CLMS(6)

6. The method of claim 1 wherein said immunoglobulin is purified from
the milk of said mammal.

CLMS(7)

7. The method of claim 1 wherein said promoter is the casein promoter.

CLMS(8)

8. A high level expression method for providing a heterologous and assembled immunoglobulin, in the milk of a transgenic goat comprising:
obtaining milk from a transgenic goat having introduced into its germline a heterologous immunoglobulin protein-coding sequence operatively linked to a promoter sequence that results in the preferential expression of said protein-coding sequence in mammary gland epithelial cells, thereby providing said heterologous and assembled immunoglobulin in the milk of said goat, wherein said heterologous and assembled immunoglobulin is a functional configuration
and is produced at levels of at least about 1 mg/ml in the milk of said goat.

CLMS(9)

9. The method of claim 8 wherein said promoter is selected from the group consisting of the beta lactoglobulin promoter, whey acid protein promoter, and the lactalbumin promoter.

CLMS(10)

10. The method of claim 8 wherein said immunoglobulin comprises heavy
and light chains.

CLMS(11)

11. The method of claim 8 wherein said immunoglobulin is of human origin.

CLMS(12)

12. The method of claim 8 wherein said immunoglobulin is purified from
the milk of said goat.

CLMS(13)

13. The method of claim 8 wherein said promoter is the casein promoter.

US PAT NO: 5,750,172 [IMAGE AVAILABLE] L15: 4 of 8

CLAIMS:

CLMS(1)

We claim:

1. Nonhuman mammal's milk comprising detectable levels of a recombinant
polypeptide chain, wherein the recombinant polypeptide chain is produced
by a nonhuman transgenic mammal whose somatic and germ cells contain an
expression system comprising a DNA sequence coding for the recombinant
polypeptide chain operably linked to a casein promoter and a signal peptide sequence, wherein the recombinant polypeptide chain is selected
from the group consisting of coagulation factors VIII and IX, tissue plasminogen activator (TPA), urokinase, growth hormone, insulin, interferons, interleukins, peptide hormones, immunoglobulins and biologically active fragments thereof.

CLMS(2)

2. The milk of claim 1, wherein the non-human mammal is selected from
the group consisting of sheep, goats, pigs and mice.

CLMS(3)

3. The milk of claim 1, wherein the expression system further comprises
a 3' untranslated region downstream of the DNA sequence coding for the
recombinant polypeptide.

CLMS(4)

4. The milk of claim 1, wherein the expression system further comprises
a 5' untranslated region between said promoter and the DNA sequence coding for the signal peptide.

CLMS(5)

5. The milk of claim 1, wherein the promoter is an .alpha.s1 casein promoter.

US PAT NO: 5,688,677 [IMAGE AVAILABLE] L15: 5 of 8

CLAIMS:

CLMS(1)

We claim:

1. Recombinant DNA comprising a nucleic acid sequence, the sequence
including:
a consensus sequence of at least one hormone responsive element, wherein
the consensus sequence is mutated to render said hormone responsive
element inactive; and
a sequence encoding a membrane-associated protein.

CLMS(2)

2. The DNA of claim 1 wherein the consensus sequence is located within
the sequence encoding the membrane-associated protein.

CLMS(3)

3. The DNA of claim 1 wherein the membrane-associated protein is cystic
fibrosis transmembrane conductance regulator.

CLMS(4)

4. The DNA of claim 2 wherein the membrane-associated protein is cystic
fibrosis transmembrane conductance regulator.

CLMS(5)

5. The DNA of claim 1 wherein the hormone responsive element is asteroid
hormone responsive element.

CLMS(6)

6. The DNA of claim 5 wherein the steroid hormone responsive element is
a glucocorticoid responsive element.

CLMS(7)

7. The DNA of claim 5 wherein the steroid hormone responsive element is
an androgen responsive element.

CLMS(8)

8. The DNA of claim 4 wherein the consensus sequence is selected from
the group of nucleotide sequences consisting of SEQ ID NO:3, SEQ ID NO:4,
SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7.

CLMS(9)

9. The DNA of claim 8 wherein the consensus sequence is an androgen
responsive element.

CLMS(10)

10. The DNA of claim 1 wherein the mutation comprises nucleotide substitution, addition or deletion.

CLMS(11)

11. A cystic fibrosis-affected cell comprising the DNA of claim 1.

US PAT NO: 5,272,254 [IMAGE AVAILABLE] L15: 6 of 8

CLAIMS:

CLMS(1)

We claim:

1. A fused protein which is produced by a host transformed with a recombinant DNA molecule comprising a hybrid DNA, the hybrid DNA coding
for the fused protein and comprising at least two DNAs joined end to end
and in the same reading frame, the first DNA coding for streptavidin or a
portion thereof, the streptavidin or portion thereof being able to bind to biotin or biotin derivatives or analogues and selected from the group consisting of:
(a) SA304, SA307, SA324;
(b) DNA which hybridizes to any of the foregoing DNA in 6XSSC and 0.1%
SDS at 30.degree. C. overnight and which codes on expression for a polypeptide which is able to bind to biotin or biotin derivatives or analogues; and
(c) DNA which, within the degeneracy of the genetic code, encodes the
same polypeptide as either (a) or (b); and said second DNA coding for
another protein, polypeptide, peptide or amino acid.

CLMS(2)

2. A fused protein, according to claim 1, wherein the protein, polypeptide, peptide or amino acid encoded by the second DNA sequence is
selected from the group consisting of human and animal interferons, human
and animal growth hormones, antigens of FMDV, antigens of HBV, human
insulin, human blood factors, tissue plasminogen activator and erythropoietin.

CLMS(3)

3. The fused protein according to claim 1, wherein the hybrid DNA further comprises a sufficient protein of a signal DNA sequence to cause
secretion of the fused protein across the cell membrane of the transformed host.

CLMS(4)

4. The fused protein according to claim 1 or 3, wherein the hybrid DNA
further comprises a sufficient portion of a signal DNA sequence to cause
maturation of the fused protein upon secretion of the fused protein across the cell membrane of the transformed host.

CLMS(5)

5. A streptavidin, or portion thereof, which is able to bind biotin or biotin derivatives or analogues, said streptavidin containing the streptavidin signal sequence or a portion thereof at the amino terminus and being produced by a host transformed with a recombinant DNA molecule
comprising a DNA coding for the streptavidin or portion thereof, the DNA
selected from the group consisting of:
(a) SA304 and SA307;
(b) DNA sequences which hybridize to any of the foregoing DNA sequences
in 6X and 0.1% SDS at 30.degree. C. overnight and which code for the
polypeptide or portion thereof, which is able to bind to biotin or
biotin derivatives or analogues; and
(c) DNA which, within the degeneracy of the genetic code, encodes the
same polypeptide as either (a) or (b).

US PAT NO: 5,168,049 [IMAGE AVAILABLE] L15: 7 of 8

CLAIMS:

CLMS(1)

We claim:

1. An isolated DNA sequence coding for streptavidin or a portion thereof, said streptavidin or portion thereof being able to bind to biotin or biotin derivatives or analogues; selected from the group consisting of:
(a) SA304, SA307, SA324;
(b) DNA sequences which hybridize to any of the foregoing DNA sequences
and which code on expression for a polypeptide which is able to bind to
biotin or biotin derivatives or analogues; and
(c) DNA sequences which code on expression for a polypeptide coded for
on expression of any of the foregoing DNA sequences.

CLMS(2)

2. The DNA sequence according to claim 1, wherein said DNA sequence
contains a sufficient portion of a signal DNA sequence to cause, upon expression of said DNA sequence, secretion of the polypeptide encoded by
said DNA sequence across the cell membrane of a unicellular host transformed with said DNA sequence.

CLMS(3)

3. The DNA sequence according to claim 2, wherein said DNA sequence
contains a sufficient portion of a signal DNA sequence to cause, upon expression of said DNA sequence, maturation of the polypeptide encoded by
said DNA sequence upon secretion of said polypeptide across the cell membrane of a unicellular host transformed with said DNA sequence.

CLMS(4)

4. A recombinant DNA molecule comprising DNA selected from the group
consisting of:
(a) a DNA sequence coding for streptavidin or a portion thereof, said streptavidin or portion thereof being able to bind biotin or biotin derivatives or analogues; selected from the group consisting of:
(1) SA304, SA307, SA324;
(2) DNA sequences which hybridize to any of the foregoing DNA sequences
and which code on expression for a polypeptide which is able to bind to biotin or biotin derivatives or analogues; and
(3) DNA sequences which code on expression for a polypeptide coded for
on expression of any of the foregoing DNA sequences;
(b) DNA comprising any of the foregoing DNA sequences and further comprising a sufficient portion of a signal DNA sequence to cause, upon
expression of said DNA sequence, secretion of the polypeptide encoded
by said DNA sequence across the cell membrane of a unicellular host transformed with said DNA sequence, and
(c) DNA comprising any of the foregoing DNA sequences and further comprising a sufficient portion of a signal DNA sequence to cause, upon
expression of said DNA sequence, maturation of the polypeptide encoded
by said DNA sequence upon secretion of said polypeptide across the cell
membrane of a unicellular host transformed with said DNA sequence.

CLMS(5)

5. The recombinant DNA molecule according to claim 4, wherein said DNA
sequence is operatively linked to an expression control sequence in said
molecule.

CLMS(6)

6. The recombinant DNA molecule according to claim 5 wherein the expression control sequence is selected from the group consisting of the
E. coli lac system, the E. coli trp system, the E. coli .beta.-lac system, the TAC system, the TRC system, the major operator and promoter
regions of bacteriophage lambda, the operator and promoter regions of filamentous single-stranded DNA phages, expression control sequences from
Streptomyces or other gram positive bacteria, and combinations thereof.

CLMS(7)

7. The recombinant DNA molecule according to claim 6, selected from the
group consisting of pSA304, pSA307 and pSA3721.

CLMS(8)

8. A unicellular host transformed with at least one recombinant DNA molecule according to claim 5, the expression control sequence in said recombinant DNA molecule being operatively linked to a DNA sequence in
said host.

CLMS(9)

9. The transformed host according to claim 8, selected from the group consisting of S. lividans (pSA3721), E. coli K12 (pSA304) and E. coli K12
(pSA307).

CLMS(10)

10. The transformed host according to claim 8, wherein the host transformed is selected from the group consisting of:
(a) bacteria;
(b) fungi;
(c) plant hosts; and
(d) animal hosts.

CLMS(11)

11. The transformed host according to claim 10, wherein the bacteria are
selected from the group consisting of:
(a) Streptomyces;
(b) Bacillus; and
(c) E. coli.

CLMS(12)

12. The transformed host according to claim 10, wherein the fungus is yeast.

CLMS(13)

13. The transformed host according to claim 10, wherein the animal host
is human tissue cells.

CLMS(14)

14. A method for producing streptavidin or a portion thereof, said streptavidin or portion thereof being able to bind to biotin or biotin derivatives or analogues, comprising the step of culturing a host transformed with a recombinant DNA molecule according to claim 4.

CLMS(15)

15. The method according to claim 14, wherein the host transformed is
selected from the group consisting of:
(a) bacteria;
(b) fungi;
(c) plant hosts; and
(d) animal hosts.

CLMS(16)

16. The method according to claim 15, wherein the bacteria are selected
from the group consisting of:

(a) Streptomyces,
(b) Bacillus; and
(c) E. coli.

CLMS(17)

17. The method according to claim 15, wherein the fungus is yeast.

CLMS(18)

18. The method according to claim 15, wherein the animal host is human
tissue cells.

CLMS(19)

19. A hybrid DNA sequence coding for a fused protein, comprising at least two DNA sequences joined end to end and in the same reading frame,
said first DNA sequence coding for streptavidin or a portion thereof, said streptavidin or portion thereof being able to bind to biotin or biotin derivatives or analogues, and selected from the group consisting of:
(a) SA304, SA307, SA324;
(b) DNA sequences which hybridize to any of the foregoing DNA sequences,
and which code on expression for a polypeptide which is able to bind to
biotin or biotin derivatives or analogues; and
(c) DNA sequences which code on expression for a polypeptide coded for
on expression of any of the foregoing DNA sequences;
and said second DNA sequence coding for another protein, polypeptide,
peptide or amino acid.

CLMS(20)

20. The hybrid DNA sequence according to claim 19, further comprising a
sufficient portion of a signal DNA sequence to cause, upon expression of
said DNA sequence, secretion of the fused protein across the cell membrane of a unicellular host transformed with said DNA sequence.

CLMS(21)

21. The hybrid DNA sequence according to claim 20, further comprising a
sufficient portion of a signal DNA sequence to cause, upon expression of
said DNA sequence, maturation of the fused protein upon secretion of said
polypeptide across the cell membrane of a unicellular host transformed with said hybrid DNA sequence.

CLMS(22)

22. A hybrid DNA sequence according to claim 19, 20 or 21, in which said
second DNA sequence codes for tissue plasminogen activator, said hybrid
DNA sequence being selected from the group consisting of:
(a) SAT9724; and
(b) SAT7021.

CLMS(23)

23. The hybrid DNA sequence according to claim 19, 20 or 21, wherein the
second DNA sequence encodes polypeptides selected from the group consisting of human interferons, human growth hormone, animal growth
hormones, antigens of FMDV, antigens of HBV, human insulin, and tissue
plasminogen activator.

CLMS(24)

24. A recombinant DNA molecule comprising a hybrid DNA sequence
according to claim 19, 20 or 21, wherein said hybrid DNA sequence is operatively linked to an expression control sequence in said molecule.

CLMS(25)

25. The recombinant DNA molecule according to claim 24, wherein said
hybrid DNA sequence contains a second DNA sequence encoding polypeptides
selected from the group consisting of human interferons, human growth
hormone, animal growth hormones, antigens of FMDV, antignes of HBV, human
insulin, and tissue plasminogen activator.

CLMS(26)

26. The recombinant DNA molecule according to claim 24, wherein the
expression control sequence is selected from the group consisting of the
E. coli lac system, the E. coli trp system, the E. coli .beta.-lac system, the TAC system, the TRC system, the major operator and promoter
regions of bacteriophage lambda, the operator and promoter regions of filamentous single-stranded DNA phages, expression control sequences from
Streptomyces or other gram positive bacteria, and combinations thereof.

CLMS(27)

27. A recombinant DNA molecule according to claim 26, selected from the
group consisting of pSAT9724 and pSAT7026.

CLMS(28)

28. A method for producing a fused protein comprising the step of culturing a host transformed with a recombinant DNA molecule of claim 24.

CLMS(29)

29. The method of claim 28, wherein the hybrid DNA sequence contains a
second DNA sequence, said second DNA sequence encoding polypeptides
selected from the group consisting of human interferons, human growth
hormone, animal growth hormones, antigens of FMDV, antigens of HBV, human
insulin, and tissue plasminogen activator.

CLMS(30)

30. A unicellular host transformed with at least one recombinant DNA molecule according to claim 24 the expression control sequence in said DNA molecule being operatively linked to a DNA sequence in said host.

CLMS(31)

31. A transformed host according to claim 30, selected from the group consisting of E. coli HB101 (pSAT9724) and S. lividans (pSAT7026).

CLMS(32)

32. The transformed host according to claim 30, wherein the host transformed is selected from the group consisting of:
(a) bacteria;
(b) fungi;
(c) plant hosts; and
(d) animal hosts.

CLMS(33)

33. The transformed host according to claim 32, wherein the bacteria are
selected from the group consisting of:
(a) Streptomyces;
(b) Bacillus; and
(c) E. coli

CLMS(34)

34. The transformed host according to claim 32, wherein the fungus is yeast.

CLMS(35)

35. The transformed host according to claim 32, wherein the animal host
is human tissue cells.

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L15: 8 of 8

CLAIMS:

CLMS(1)

We claim:

1. A process for the production and secretion into mammal's milk of an
exogenous recombinate protein comprising the steps of:
a. producing milk in a transgenic mammal characterized by an expression
system comprising a casein promoter operatively linked to an exogenous
DNA sequence coding for the recombinant protein through a DNA sequence
coding for a signal peptide effective in secreting and maturing the
recombinant protein in mammary tissue;
b. collecting the milk; and
c. isolating the exogenous recombinant protein from the milk.

CLMS(2)

2. The process according to claim 1, wherein said expression system also
includes a 3' untranslated region downstream of the DNA sequence coding
for the recombinant protein.

CLMS(3)

3. The process according to claim 1, wherein said expression system also
includes a 5' untranslated region between said promoter and the DNA
sequence coding for the signal peptide.

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L1 107 S MAMMARY(10A)(IMMUNOGLOB? OR ANTIBOD?)
L2 80 S L1 AND MILK
L3 69 S L2 AND EXPRESS?
L4 42 S L3 AND (VECTOR# OR CONSTRUCT# OR PLASMID#)
L5 296 S MAMMARY(5A)(PROMOTER#)
L6 1 S L5(10A)(ANTIBOD? OR IMMUNOGLOB?)
L7 59 S L5 AND (CASEIN# OR WHEY ACID OR LACTALBUMIN OR LACTOGLOB
ULI
L8 55 S L7 AND (IMMUNOGLOB? OR ANTIBOD?)
L9 44 S L8 AND MILK
L10 359 S MAMMARY(10A)(PROMOTER#)
L11 40 S L10(10A)(MILK)
L12 0 S L11(10A)(ANTIBOD? OR IMMUNOGLOB?)
L13 37 S L10(P)(ANTIBOD? OR IMMUNOGLOB?)
L14 20 S L13(P)(MILK)
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=> s immunoglob?

L1      11569 IMMUNOGLOB?

=> s l1 and whey acidic protein

        4328 WHEY
       98021 ACIDIC
       73025 PROTEIN
          45 WHEY ACIDIC PROTEIN
             (WHEY(W)ACIDIC(W)PROTEIN)
L2        18 L1 AND WHEY ACIDIC PROTEIN

=> s l2 and promoter#

       36024 PROMOTER#
L3        16 L2 AND PROMOTER#

=> s l3 and (construct# or vector# or plasmid#)

       96404 CONSTRUCT#
       77317 VECTOR#
       16546 PLASMID#
L4        16 L3 AND (CONSTRUCT# OR VECTOR# OR
PLASMID#)

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1. 5,919,997, Jul. 6, 1999, Transgenic mice having modified cell-cycle regulation; David H. Beach, et al., 800/18; 435/91.2, 320.1, 325, 455, 463, 467; 800/3, 22, 25 [IMAGE AVAILABLE]

US PAT NO: 5,919,997 [IMAGE AVAILABLE] L4: 1 of 16

ABSTRACT:
The present invention relates to transgenic mice in which the biological
function of at least one cell cycle regulatory proteins of the INK4 family is altered.

2. 5,912,142, Jun. 15, 1999, Gene product over expressed in cancer cells; Russel E. Kaufman, et al., 435/69.1, 252.3, 320.1, 325; 530/350; 536/23.1, 23.5 [IMAGE AVAILABLE]

US PAT NO: 5,912,142 [IMAGE AVAILABLE] L4: 2 of 16

ABSTRACT:
The present invention relates, in general, to a cancer-related protein and to a nucleic acid sequence encoding same. In particular, the invention relates to a protein over expressed in certain neoplastic cells, including breast and ovarian cancer cells, to its encoding sequence, and to diagnostic and treatment methodologies based on same.

3. 5,892,070, Apr. 6, 1999, Transgenic non-human mammals producing
oligosaccharides and glycoconjugates; Pedro Antonio Prieto, et al., 800/14; 435/69.1; 800/15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,892,070 [IMAGE AVAILABLE] L4: 3 of 16

ABSTRACT:
The invention relates to transgenic non-human mammals characterized in
that the genome of said mammals contain at least one heterologous gene
encoding for the production of heterologous catalytic entity selected from the group consisting of enzymes and antibodies, and wherein said catalytic entity produces a second heterologous product in the milk of said mammal. Especially useful in the practice of the invention are human
glycosyltransferases and transgenic sheep, goats and cows. The heterologous product includes oligosaccharides and glycoconjugates. Specifically exemplified, is the production of 2'-fucosyl-lactose in the milk of transgenic mice which contain and express a transgene encoding
.alpha.-1,2-fucosyltransferase operatively linked to a mammary gland specific **promoter**.

4. 5,891,698, Apr. 6, 1999, Oligosaccharides and glycoproteins produced
in milk of transgenic non-human mammals; Pedro Antonio Prieto, et al.,
800/7; 435/100; 800/14, 15, 16, 17, 18, 25 [IMAGE AVAILABLE]

US PAT NO: 5,891,698 [IMAGE AVAILABLE] L4: 4 of 16

ABSTRACT:
The invention relates to humanized milk. The milk is produced by a non-human transgenic mammal wherein the genome of said transgenic non-human mammal contains at least one heterologous gene encoding for a
human catalytic entity and wherein the catalytic entity produces oligosaccharides and glycoconjugates that are present in the milk of said transgenic non-human mammal. An especially useful catalytic entity is human glycosyltransferases which produce oligosaccharides and glyconjugates. Specifically exemplified, is the production of 2'-fucosyl-lactose in the milk of transgenic mice which contain and express a transgene encoding .alpha.-1,2-fucosyltransferase operatively linked to a mammary gland specific **promoter**. A method of obtaining
humanized milk is disclosed. The method comprises the steps of (a) inserting into the genome of a non-human mammal a heterologous gene
encoding the production of a human catalytic entity wherein said catalytic entity produces a secondary gene product in the milk of said non-human mammal; and (b) milking said non-human mammal. The humanized
milk may be used in the preparation of an enteral nutritional product useful in the nutritive maintenance of an animal.

5. 5,888,774, Mar. 30, 1999, Recombinant DNA molecules and expression
vectors for erythropoietin; Genevieve Delcuve, 435/69.6, 320.1, 455,
456 [IMAGE AVAILABLE]

US PAT NO: 5,888,774 [IMAGE AVAILABLE] L4: 5 of 16

ABSTRACT:
A recombinant DNA molecule adapted for transfection of a host cell comprising a nucleic acid molecule encoding mammalian erythropoietin, an
expression control sequence operatively linked thereto and at least one SAR element. The invention also relates to expression **vectors** having
the recombinant DNA molecule and to mammalian cells transformed with the
expression **vector**. The mammalian cells lack multiple copies of an
amplified amplification gene and are capable of expressing recombinant
EPO in vitro at levels of at least 1,500 u/10.sup.6 cells in 24 hours. The invention further relates to a method of expressing recombinant mammalian erythropoietin using the expression **vectors** and to a transgenic non-human animal or embryo whose germ cells and somatic cells
contain a DNA **construct** having the recombinant DNA molecule of the
invention.

6. 5,833,982, Nov. 10, 1998, Modified factor VII; Kathleen L. Berkner,
et al., 424/94.64; 435/212, 226; 514/12; 530/384 [IMAGE AVAILABLE]

US PAT NO: 5,833,982 [IMAGE AVAILABLE] L4: 6 of 16

ABSTRACT:

The catalytic active site of Factor VII is modified to produce a compound
which effectively interrupts the blood coagulation cascade. The modifications render Factor VIIa substantially unable to activate plasma
Factors X or IX. Pharmaceutical compositions of the modified Factor VII
are used to treat a variety of coagulation-related disorders, including platelet deposition, vascular thrombosis, ischemic reperfusion, acute closure of a coronary artery, vascular restenosis secondary to balloon angioplasty, endarterectomy, reductive atherectomy, stent placement, laser therapy or rotablation.

7. 5,817,788, Oct. 6, 1998, Modified factor VII; Kathleen L. Berkner, et
al., 536/23.2; 435/212, 226, 325 [IMAGE AVAILABLE]

US PAT NO: 5,817,788 [IMAGE AVAILABLE] L4: 7 of 16

ABSTRACT:
The catalytic active site of Factor VII is modified to produce a compound
which effectively interrupts the blood coagulation cascade. The modifications render Factor VIIa substantially unable to activate plasma
Factors X or IX. Pharmaceutical compositions of the modified Factor VII
are used to treat a variety of coagulation-related disorders.

8. 5,788,965, Aug. 4, 1998, Modified factor VII; Kathleen L. Berkner, et
al., 424/94.64; 435/212, 226; 514/12, 822; 530/384 [IMAGE AVAILABLE]

US PAT NO: 5,788,965 [IMAGE AVAILABLE] L4: 8 of 16

ABSTRACT:
The catalytic active site of Factor VII is modified to produce a compound
which effectively interrupts the blood coagulation cascade. The modifications render Factor VIIa substantially unable to activate plasma
Factors X or IX. Pharmaceutical compositions of the modified Factor VII
are used to treat a variety of coagulation-related disorders.

9. 5,776,773, Jul. 7, 1998, Yeast artificial chromosomes and their use in the control of gene expression; Marianne Bruggemann, 435/325, 320.1,
449 [IMAGE AVAILABLE]

US PAT NO: 5,776,773 [IMAGE AVAILABLE] L4: 9 of 16

ABSTRACT:
Embryonic stem cells that are essentially free of yeast DNA are prepared
from suitably marked yeast artificial chromosomes and used to transfer DNA segments of considerable size into organisms.

10. 5,750,176, May 12, 1998, Transgenic non-human mammal milk comprising
2'-fucosyl-lactose; Pedro Antonio Prieto, et al., 426/580; 424/530; 426/556, 587, 588; 530/832; 800/7 [IMAGE AVAILABLE]

US PAT NO: 5,750,176 [IMAGE AVAILABLE] L4: 10 of 16

ABSTRACT:
The invention relates to the milk of a transgenic non-human mammal. The
milk is characterized in that it contains heterologous components produced as the secondary gene products of a heterologous gene contained
in the genome of the transgenic non-human mammal. The heterologous gene
encodes a heterologous catalytic entity such as a human enzyme selected
from the group consisting of glycosyltransferases, phosphorylases, hydroxylases, peptidases and sulfotransferases. Especially useful in the practice of the invention are human glycosyltransferases. The desired heterologous components include oligosaccahrides, glycoconjugates. Specifically exemplified, is the production of 2'-fucosyl-lactose in the milk of transgenic mice which contain and express a transgene encoding
.alpha.-1,2-fucosyltransferase operatively linked to a mammary gland specific **promoter**. The oligosaccahrides and glycoconjugates may be
isolated from the milk of the transgenic mammals and used in the preparation of pharmaceuticals, diagnostic kits, nutritional products and
the like. The whole transgenic milk may also be used to formulate nutritional products that provide special advantages. The transgenic milk
may also be used in the production of specialized enteral nutritional products.

11. 5,700,671, Dec. 23, 1997, Methods of making transgenic animals producing oligosaccharides and glycoproteins; Pedro Antonio Prieto, et al., 800/25; 435/6, 69.1, 193 [IMAGE AVAILABLE]

US PAT NO: 5,700,671 [IMAGE AVAILABLE] L4: 11 of 16

ABSTRACT:
The invention relates to transgenic non-human mammals characterized in
that the genome of said mammals contain at least one heterologous gene
encoding for the production of heterologous catalytic entity selected from the group consisting of enzymes and antibodies, and wherein said catalytic entity produces a second heterologous product in the milk of said mammal. Especially useful in the practice of the invention are human
glycosyltransferases and transgenic sheep, goats and cows. The heterologous product includes oligosaccharides and glycoconjugates.

12. 5,648,243, Jul. 15, 1997, Human serum albumin expression **construct**; David R. Hurwitz, et al., 435/69.6, 320.1; 536/23.1, 23.5,
24.1, 24.2 [IMAGE AVAILABLE]

US PAT NO: 5,648,243 [IMAGE AVAILABLE] L4: 12 of 16

ABSTRACT:
The present invention provides DNA **constructs** comprising a **promoter** DNA sequence and a DNA sequence coding for human serum
albumin. In one embodiment the human serum albumin sequence comprises at
least one, but not all, of the introns in the naturally occurring gene encoding for the HSA protein. In another embodiment the DNA **constructs** comprise a 5' regulatory sequence which directs the expression and secretion of HSA protein in the milk of a transgenic animal. Preferably, the **promoter** gene is a milk protein **promoter**
sequence such as .beta.-lactoglobulin. The present invention also provides transgenic animals which secrete HSA in the milk of lactating females. The present invention also provides **vectors** comprising the
constructs of the present invention.

13. 5,476,995, Dec. 19, 1995, Peptide production; Anthony J. Clark, et
al., 800/16; 435/69.1, 317.1, 320.1 [IMAGE AVAILABLE]

US PAT NO: 5,476,995 [IMAGE AVAILABLE] L4: 13 of 16

ABSTRACT:
A method of producing a proteinaceous compound, involves incorporating a
DNA sequence coding for polypeptide into a gene of a mammal (such as a
sheep) coding for a milk whey protein in such a way that the DNA sequence
is expressed in the mammary gland of the adult female mammal. The proteinaceous compound may be a (optionally modified) protein such as a
blood coagulation factor. The DNA sequence is preferably inserted into
the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The proteinaceous compound will generally be recovered from milk of the female mammal, but may (for example if it is
an enzyme) be used in situ.

14. 5,366,894, Nov. 22, 1994, Peptide production; Anthony J. Clark, et
al., 435/320.1, 69.1, 325 [IMAGE AVAILABLE]

US PAT NO: 5,366,894 [IMAGE AVAILABLE] L4: 14 of 16

ABSTRACT:
A method of producing a substance comprising a peptide, involves incorporating a DNA sequence coding for the peptide into a gene of a mammal (such as a sheep) coding for a milk whey protein in such a way
that the DNA sequence is expressed in the mammary gland of the adult
female mammal. The substance may be an (optionally modified) protein such
as a blood coagulation factor. The DNA sequence is preferably inserted
into the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The substance will generally be recovered from milk
of the female mammal, but may (for example if it is an enzyme) be used in
situ.

15. 5,322,775, Jun. 21, 1994, Peptide production; Anthony J. Clark, et al., 435/69.1, 69.6, 69.7, 317.1, 320.1; 530/412 [IMAGE AVAILABLE]

US PAT NO: 5,322,775 [IMAGE AVAILABLE] L4: 15 of 16

ABSTRACT:
A method of producing a proteinaceous compound, involves incorporating a
DNA sequence coding for a polypeptide chain of said compound into a gene
of a mammal (such as a sheep) coding for a milk whey protein in such a
way that the DNA sequence is expressed in the mammary gland of the adult
female mammal. The proteinaceous compound may be a (optionally modified)
protein such as a blood coagulation factor. The DNA sequence is preferably inserted into the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The proteinaceous compound will generally be recovered from milk of the female mammal, but may (for example if it is an enzyme) be used in situ.

16. 5,221,778, Jun. 22, 1993, Multiplex gene regulation; Guerard W. Byrne, et al., 800/4; 424/231.1; 435/193, 317.1, 948; 800/18, 22 [IMAGE
AVAILABLE]

US PAT NO: 5,221,778 [IMAGE AVAILABLE] L4: 16 of 16

ABSTRACT:
A transgenic mouse offspring produced by the mating of a first transgenic
mouse carrying a transresponder transgene whose expression is regulated
by a viral gene product of HSV-1 and a second transgenic mouse carrying a
transactivator transgene. A process for expressing a gene of interest which comprises the mating of a first transgenic mouse carrying a transresponder transgene whose expression is regulated by a viral gene product of HSV-1 and a second transgenic mouse carrying a transactivator
transgene.

=> s immunoglob? and casein

11569 IMMUNOGLOB?
17607 CASEIN
L5 908 IMMUNOGLOB? AND CASEIN

=> s l5 and promoter#

36024 PROMOTER#
L6 410 L5 AND PROMOTER#

=> s l6 and (construct# or vector# or plasmid#)

96404 CONSTRUCT#
77317 VECTOR#
16546 PLASMID#
L7 387 L6 AND (CONSTRUCT# OR VECTOR# OR PLASMID#)

=> s immunoglob? and casein promoter

11569 IMMUNOGLOB?
17607 CASEIN
27862 PROMOTER
34 CASEIN PROMOTER
(CASEIN(W)PROMOTER)
L8 20 IMMUNOGLOB? AND CASEIN PROMOTER

=> d 1- cit ab

1. 5,928,904, Jul. 27, 1999, DNA encoding recombinant IL4 antibodies
useful in treatment of IL4 mediated disorders; Stephen D. Holmes, et al.,
435/69.6, 70.21, 71.1, 320.1, 326, 328, 335; 530/300, 350, 387.3, 388.23;
536/23.5, 23.53 [IMAGE AVAILABLE]

US PAT NO: 5,928,904 [IMAGE AVAILABLE] L8: 1 of 20

ABSTRACT:
Chimeric and humanized IL4 MAbs derived from high affinity MAbs, pharmaceutical compositions containing same, and methods of treatment are
provided.

2. 5,914,110, Jun. 22, 1999, Recombinant IL4 antibodies useful in treatment of IL4 mediated disorders; Stephen D. Holmes, et al., 424/133.1, 141.1, 152.1; 435/7.1, 70.21, 326, 328, 335; 530/350, 387.3,
388.15, 388.23, 391.1 [IMAGE AVAILABLE]

US PAT NO: 5,914,110 [IMAGE AVAILABLE] L8: 2 of 20

ABSTRACT:
Chimeric and humanized IL4 MAbs derived from high affinity MAbs, pharmaceutical compositions containing same, and methods of treatment are
provided.

3. 5,877,010, Mar. 2, 1999, Thymidine kinase mutants; Lawrence A. Loeb,
et al., 435/320.1, 243, 325; 536/23.2, 23.5, 23.72, 24.1 [IMAGE AVAILABLE]

US PAT NO: 5,877,010 [IMAGE AVAILABLE] L8: 3 of 20

ABSTRACT:
The present invention provides isolated nucleic acid molecules encoding a
Herpesviridae thymidine kinase enzyme comprising one or more mutations,
at least one of the mutations encoding an amino acid substitution upstream from a DRH nucleoside binding site which increases a biological
activity of the thymidine kinase, as compared to unmutated thymidine kinase. Within another aspect, one of the mutations is an amino acid substitution within a DRH nucleoside binding site which increases a biological activity of the thymidine kinase, as compared to unmutated thymidine kinase. Also provided are vectors suitable for expressing such
DNA molecules, as well as methods for utilizing such vectors.

4. 5,851,525, Dec. 22, 1998, Recombinant IL-5 antagonists useful in treatment of IL-5 mediated disorders; Robert S. Ames, Jr., et al., 424/145.1, 152.1, 158.1, 172.1; 530/387.1, 387.3, 388.23 [IMAGE AVAILABLE]

US PAT NO: 5,851,525 [IMAGE AVAILABLE] L8: 4 of 20

ABSTRACT:
Chimeric, humanized and other IL-5 mAbs, derived from high affinity neutralizing mAbs, pharmaceutical compositions containing same, methods
of treatment and diagnostics are provided.

5. 5,849,992, Dec. 15, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/14, 7, 15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L8: 5 of 20

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

6. 5,827,690, Oct. 27, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/7; 530/867 [IMAGE AVAILABLE]

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L8: 6 of 20

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

7. 5,783,184, Jul. 21, 1998, Method for treatment and diagnosis of IL-5
mediated disorders; Edward Robert Appelbaum, et al., 424/130.1, 133.1,
141.1, 145.1; 435/7.1; 530/388.1, 388.23 [IMAGE AVAILABLE]

US PAT NO: 5,783,184 [IMAGE AVAILABLE] L8: 7 of 20

ABSTRACT:
The present invention relates to treatment and diagnosis of conditions mediated by IL-5 and excess eosinophil production, and more specifically
to mAbs and other altered antibodies such as Fabs, chimeric, human and
humanized antibodies that do not block binding of human IL-5 to the .alpha.-chain of the human IL-5 receptor.

8. 5,750,172, May 12, 1998, Transgenic non human mammal milk; Harry
Meade, et al., 426/580; 435/69.1, 69.4, 69.51, 69.52, 69.6, 183, 215; 800/7 [IMAGE AVAILABLE]

US PAT NO: 5,750,172 [IMAGE AVAILABLE] L8: 8 of 20

ABSTRACT:
This invention relates to the production of recombinant proteins, such as
coagulation factors VIII and IX, tissue plasminogen activator (TPA), urokinase, growth hormone, insulin, interferons, interleukins, peptide hormones and **immunoglobulins**, in mammals' milk. Particularly, this
invention relates to an expression system which when transgenically incorporated into a mammal permits the female species of that mammal to
produce the desired recombinant protein in or along with its milk. This invention also relates to the transgenic mammal that produces the desired
recombinant product in its milk.

9. 5,741,957, Apr. 21, 1998, Transgenic bovine; Herman A. Deboer, et
al., 800/7; 435/69.1; 800/15, 25 [IMAGE AVAILABLE]

US PAT NO: 5,741,957 [IMAGE AVAILABLE] L8: 9 of 20

ABSTRACT:
A transgenic bovine is disclosed whose somatic and germ cells contain a
transgene, wherein the transgene comprising a mammary gland specific promoter, a mammary gland specific enhancer, a DNA sequence encoding a
signal sequence functional in bovine mammary gland secretory cells and a
DNA sequence encoding a heterologous polypeptide of interest wherein the
transgenic bovine expresses the transgene such that the polypeptide of interest is detectable in milk produced by the transgenic bovine.

10. 5,736,388, Apr. 7, 1998, Bacteriophage-mediated gene transfer systems capable of transfecting eukaryotic cells; Sunil Chada, et al., 435/320.1; 424/93.6; 435/235.1; 514/44 [IMAGE AVAILABLE]

US PAT NO: 5,736,388 [IMAGE AVAILABLE] L8: 10 of 20

ABSTRACT:
Lamboid bacteriophage capable of specifically interacting with and delivering nucleic acid molecules to eukaryotic cells are disclosed. Such
bacteriophage-derived gene transfer systems target one or more specific
receptors on eukaryotic cells, for instance by incorporating mutant tail fiber proteins or by incorporating known ligands for specific eukaryotic receptors into lambda phage. Also disclosed are methods for identifying
and producing modified bacteriophage tail fiber polypeptides capable of
specifically interacting with eukaryotic transmembrane proteins. Methods
of treating diseases using such gene transfer systems are also disclosed.

11. 5,721,367, Feb. 24, 1998, Homologous recombination in mammalian
cells; Robert M. Kay, et al., 800/18; 435/69.1, 69.7, 463, 465; 800/15 [IMAGE AVAILABLE]

US PAT NO: 5,721,367 [IMAGE AVAILABLE] L8: 11 of 20

ABSTRACT:
The invention relates to methods for intracellularly producing DNA segments by homologous recombination of smaller overlapping DNA fragments
and transgenic mammalian cells and transgenic non-human mammals produced
by such methods.

12. 5,693,323, Dec. 2, 1997, Recombinant IL-5 antagonists useful in treatment of IL-5 mediated disorders; Robert S. Ames, Jr., et al., 424/145.1; 435/328, 335; 530/387.3, 388.23 [IMAGE AVAILABLE]

US PAT NO: 5,693,323 [IMAGE AVAILABLE] L8: 12 of 20

ABSTRACT:
Chimeric, humanized and other IL-5 mAbs, derived from high affinity neutralizing mAbs, pharmaceutical compositions containing same, methods
of treatment and diagnostics are provided.

13. 5,688,677, Nov. 18, 1997, Deoxyribonucleic acids containing inactivated hormone responsive elements; Karl M. Ebert, et al., 536/23.5,
24.1 [IMAGE AVAILABLE]

US PAT NO: 5,688,677 [IMAGE AVAILABLE] L8: 13 of 20

ABSTRACT:
A DNA comprising at least one inactivated hormone responsive element and
a nucleic acid sequence encoding a membrane-associated protein is described. Therapeutic compositions and cells including the DNA are also
described. Other aspects of the invention include methods of treating subjects having cystic fibrosis which include administering an effective amount of the DNA to subjects having cystic fibrosis such that functional
cystic fibrosis transmembrane conductance regulator is produced by the
subject at a level which is not detrimental to the subject. The present invention also pertains to a method of introducing the DNA into a cell such that the membrane-associated protein is produced at a level which is
not detrimental to the cell and cells produced by this method. Still other aspects of the invention include a method of assaying DNA for the
presence or absence of a hormone responsive element in a species in which
the hormone responsive element is functional and a method of selectively
breeding female transgenic mammals which produce a protein of

interest.

14. 5,683,892, Nov. 4, 1997, DNA encoding recombinant IL-5 antagonists
useful in treatment of IL-5 mediated disorders; Robert S. Ames, Jr., et al., 435/69.1, 69.3, 70.21, 252.3, 320.1, 328; 536/23.53 [IMAGE AVAILABLE]

US PAT NO: 5,683,892 [IMAGE AVAILABLE] L8: 14 of 20

ABSTRACT:
DNA encoding chimeric, humanized and other IL-5 mAbs, derived from high
affinity neutralizing mAbs, pharmaceutical compositions containing same,
methods of treatment and diagnostics are provided.

15. 5,681,746, Oct. 28, 1997, Retroviral delivery of full length factor VIII; Mordechai Bodner, et al., 435/350, 320.1, 366, 371; 536/23.5 [IMAGE
AVAILABLE]

US PAT NO: 5,681,746 [IMAGE AVAILABLE] L8: 15 of 20

ABSTRACT:
Retroviral vectors for directing expression of full length factor VIII in transduced host cells, plasmids encoding the same, and host cells transformed, transfected, or transduced therewith are disclosed. Also disclosed are retroviral particles comprising such retrovital vectors, as are methods for making such particles in suitable packaging cells. Retroviral particles so produced may be amphotropic, ecotropic, polytropic, or xenotropic; alternatively, they may comprise chimeric or hybrid envelope proteins to alter host range. Also described are retrovital particles comprising retroviral vectors for directing full length factor VIII expression which are complement resistant. Pharmaceutical compositions comprising retrovital particles of the invention are also disclosed, as are methods of treating mammals, particularly humans, afflicted with hemophilia.

16. 5,633,076, May 27, 1997, Method of producing a transgenic bovine or
transgenic bovine embryo; Herman A. DeBoer, et al., 800/25 [IMAGE AVAILABLE]

US PAT NO: 5,633,076 [IMAGE AVAILABLE] L8: 16 of 20

ABSTRACT:
A method is disclosed for the production of a transgenic bovine or a transgenic bovine embryo comprising obtaining an ovum from bovine ovaries, maturing the ovum in vitro, fertilizing the mature ovum or ova in vitro to form a zygote, introducing a transgene into the zygote in vitro and maturing the zygote to a preimplantation stage embryo in vitro.
To produce the transgenic bovine, the embryo is transplanted into a recipient female bovine, wherein the female bovine gestates the embryo to
produce a transgenic bovine.

17. 5,612,205, Mar. 18, 1997, Homologous recombination in mammalian
cells; Robert M. Kay, et al., 435/463, 465 [IMAGE AVAILABLE]

US PAT NO: 5,612,205 [IMAGE AVAILABLE] L8: 17 of 20

ABSTRACT:

The invention relates to methods for intracellularly producing DNA segments by homologous recombination of smaller overlapping DNA fragments
and transgenic mammalian cells and transgenic non-human mammals produced
by such methods.

18. 5,525,708, Jun. 11, 1996, Covalent dimer of kit ligand; Karl H. Nocka, et al., 530/409, 351, 399, 417 [IMAGE AVAILABLE]

US PAT NO: 5,525,708 [IMAGE AVAILABLE] L8: 18 of 20

ABSTRACT:
A modified form of KL, the ligand for the c-Kit proto-oncogene, has been
prepared wherein the protein is stabilized by an intermolecular covalent
linkage. The protein can be prepared by expression of a recombinant protein which is dissolved in denaturant and refolded under conditions resulting in a disulfide linked dimer. Examples demonstrate the purification and characterization of this disulfide-linked cysteine dimer kit ligand (KL-CD) which contains at least one intermolecular disulfide
bond and has at least ten-fold greater activity in promoting cell proliferation than native, non-covalently linked KL, as measured in in vitro assays.

19. 5,268,275, Dec. 7, 1993, Vitamin K-dependent carboxylase; Darrel W.
Stafford, et al., 435/69.1, 69.6, 232, 252.3, 320.1, 352, 354, 358, 366; 536/23.2 [IMAGE AVAILABLE]

US PAT NO: 5,268,275 [IMAGE AVAILABLE] L8: 19 of 20

ABSTRACT:
Isolated DNA encoding a vitamin K dependent carboxylase is disclosed. The
carboxylase is selected from the group consisting of: (a) isolated DNA which encodes bovine or human vitamin K dependent carboxylase; (b) isolated DNA which hybridizes to isolated DNA of (a) above and which
encodes a vitamin K dependent carboxylase; and (c) isolated DNA differing
from the isolated DNAs of (a) and (b) above in nucleotide sequence due to
the degeneracy of the genetic code, and which encodes a vitamin K dependent carboxylase. Also disclosed are vectors and host cells containing the aforesaid DNA, methods of using the same, and purified
protein coded for by the aforesaid DNA.

20. 4,873,316, Oct. 10, 1989, Isolation of exogenous recombinant proteins from the milk of transgenic mammals; Harry Meade, et al., 800/7;
435/69.1, 69.2, 69.4, 69.5, 69.6, 69.8; 530/360, 361, 416, 417, 418, 832,
833; 536/23.1, 23.4, 23.5; 800/18 [IMAGE AVAILABLE]

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L8: 20 of 20

ABSTRACT:
This invention relates to the production of recombinant proteins in mammals' milk. Particularly, this invention relates to an expression system comprising the mammal's **casein** **promoter** which when
transgenically incorporated into a mammal permits the female species of
that mammal to produce the desired recombinant protein in or along with
its milk. This invention also relates to the transgenic mammal that produces the desired recombinant product in its milk.

=> d his

(FILE 'USPAT' ENTERED AT 17:22:03 ON 04 AUG 1999)
L1 11569 S IMMUNOGLOB?
L2 18 S L1 AND WHEY ACIDIC PROTEIN
L3 16 S L2 AND PROMOTER#
L4 16 S L3 AND (CONSTRUCT# OR VECTOR# OR PLASMID#)
L5 908 S IMMUNOGLOB? AND CASEIN
L6 410 S L5 AND PROMOTER#
L7 387 S L6 AND (CONSTRUCT# OR VECTOR# OR PLASMID#)
L8 20 S IMMUNOGLOB? AND CASEIN PROMOTER

=> s immunoglob? and lactoglobulin

11569 IMMUNOGLOB?
635 LACTOGLOBULIN
L9 208 IMMUNOGLOB? AND LACTOGLOBULIN

=> s immunoglob? and lactoglobulin promoter

11569 IMMUNOGLOB?
635 LACTOGLOBULIN
27862 PROMOTER

15 LACTOGLOBULIN PROMOTER
(LACTOGLOBULIN(W)PROMOTER)
L10 8 IMMUNOGLOB? AND LACTOGLOBULIN PROMOTER

=> d l- cit ab

1. 5,849,992, Dec. 15, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/14, 7, 15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L10: 1 of 8

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

2. 5,827,690, Oct. 27, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/7; 530/867 [IMAGE AVAILABLE]

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L10: 2 of 8

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

3. 5,750,172, May 12, 1998, Transgenic non human mammal milk; Harry
Meade, et al., 426/580; 435/69.1, 69.4, 69.51, 69.52, 69.6, 183, 215; 800/7 [IMAGE AVAILABLE]

US PAT NO: 5,750,172 [IMAGE AVAILABLE] L10: 3 of 8

ABSTRACT:
This invention relates to the production of recombinant proteins, such as
coagulation factors VIII and IX, tissue plasminogen activator (TPA), urokinase, growth hormone, insulin, interferons, interleukins, peptide hormones and **immunoglobulins**, in mammals' milk. Particularly, this
invention relates to an expression system which when transgenically incorporated into a mammal permits the female species of that mammal to
produce the desired recombinant protein in or along with its milk. This invention also relates to the transgenic mammal that produces the desired
recombinant product in its milk.

4. 5,648,243, Jul. 15, 1997, Human serum albumin expression construct;
David R. Hurwitz, et al., 435/69.6, 320.1; 536/23.1, 23.5, 24.1, 24.2 [IMAGE AVAILABLE]

US PAT NO: 5,648,243 [IMAGE AVAILABLE] L10: 4 of 8

ABSTRACT:
The present invention provides DNA constructs comprising a promoter DNA
sequence and a DNA sequence coding for human serum albumin. In one
embodiment the human serum albumin sequence comprises at least one, but
not all, of the introns in the naturally occurring gene encoding for the HSA protein. In another embodiment the DNA constructs comprise a 5'
regulatory sequence which directs the expression and secretion of HSA protein in the milk of a transgenic animal. Preferably, the promoter gene
is a milk protein promoter sequence such as .beta.-lactoglobulin. The present invention also provides transgenic animals which secrete HSA in
the milk of lactating females. The present invention also provides vectors comprising the constructs of the present invention.

5. 5,476,995, Dec. 19, 1995, Peptide production; Anthony J. Clark, et al., 800/16; 435/69.1, 317.1, 320.1 [IMAGE AVAILABLE]

US PAT NO: 5,476,995 [IMAGE AVAILABLE] L10: 5 of 8

ABSTRACT:
A method of producing a proteinaceous compound, involves incorporating a
DNA sequence coding for polypeptide into a gene of a mammal (such as a
sheep) coding for a milk whey protein in such a way that the DNA sequence
is expressed in the mammary gland of the adult female mammal. The proteinaceous compound may be a (optionally modified) protein such as a
blood coagulation factor. The DNA sequence is preferably inserted into
the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The proteinaceous compound will generally be recovered from milk of the female mammal, but may (for example if it is
an enzyme) be used in situ.

6. 5,366,894, Nov. 22, 1994, Peptide production; Anthony J. Clark, et al., 435/320.1, 69.1, 325 [IMAGE AVAILABLE]

US PAT NO: 5,366,894 [IMAGE AVAILABLE] L10: 6 of 8

ABSTRACT:
A method of producing a substance comprising a peptide, involves incorporating a DNA sequence coding for the peptide into a gene of a mammal (such as a sheep) coding for a milk whey protein in such a way
that the DNA sequence is expressed in the mammary gland of the adult
female mammal. The substance may be an (optionally modified) protein such
as a blood coagulation factor. The DNA sequence is preferably inserted
into the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The substance will generally be recovered from milk
of the female mammal, but may (for example if it is an enzyme) be used in
situ.

7. 5,322,775, Jun. 21, 1994, Peptide production; Anthony J. Clark, et al., 435/69.1, 69.6, 69.7, 317.1, 320.1; 530/412 [IMAGE AVAILABLE]

US PAT NO: 5,322,775 [IMAGE AVAILABLE] L10: 7 of 8

ABSTRACT:
A method of producing a proteinaceous compound, involves incorporating a
DNA sequence coding for a polypeptide chain of said compound into a gene
of a mammal (such as a sheep) coding for a milk whey protein in such a
way that the DNA sequence is expressed in the mammary gland of the adult
female mammal. The proteinaceous compound may be a (optionally modified)
protein such as a blood coagulation factor. The DNA sequence is preferably inserted into the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The proteinaceous compound will generally be recovered from milk of the female mammal, but may (for example if it is an enzyme) be used in situ.

8. 4,873,316, Oct. 10, 1989, Isolation of exogenous recombinant proteins
from the milk of transgenic mammals; Harry Meade, et al., 800/7; 435/69.1, 69.2, 69.4, 69.5, 69.6, 69.8; 530/360, 361, 416, 417, 418, 832,
833; 536/23.1, 23.4, 23.5; 800/18 [IMAGE AVAILABLE]

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L10: 8 of 8

ABSTRACT:
This invention relates to the production of recombinant proteins in mammals' milk. Particularly, this invention relates to an expression system comprising the mammal's casein promoter which when transgenically
incorporated into a mammal permits the female species of that

mammal to
produce the desired recombinant protein in or along with its milk. This invention also relates to the transgenic mammal that produces the desired
recombinant product in its milk.

=> s l1 and lactalbumin

1127 LACTALBUMIN
L11 249 L1 AND LACTALBUMIN

=> s l1 and lactalbumin promoter#

1127 LACTALBUMIN
36024 PROMOTER#
7 LACTALBUMIN PROMOTER#
(LACTALBUMIN(W)PROMOTER#)
L12 2 L1 AND LACTALBUMIN PROMOTER#

=> d l- cit ab

1. 5,849,992, Dec. 15, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/14, 7, 15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L12: 1 of 2

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

2. 5,827,690, Oct. 27, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/7; 530/867 [IMAGE AVAILABLE]

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L12: 2 of 2

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

=> d l 2 clms

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L12: 1 of 2

CLAIMS:

CLMS(1)

What is claimed is:

1. A transgenic non-human mammal all of whose germ cells and somatic
cells contain a heterologous **immunoglobulin** protein-coding sequence
operatively linked to a promoter sequence that directs the preferential expression of said protein-coding sequence in mammary gland epithelial
cells, thereby providing a heterologous and assembled **immunoglobulin**
in the milk of said mammal wherein said heterologous and assembled **immunoglobulin** is in a functional configuration and is produced at
levels of at least about 1 mg/ml in the milk of said mammal.

CLMS(2)

2. The transgenic mammal of claim 1 wherein said **immunoglobulin**
comprises a tetrameric antibody directed against a pathogen.

CLMS(3)

3. The transgenic mammal of claim 1 wherein said **immunoglobulin**
comprises a tetrameric antibody directed against a biologically active peptide.

CLMS(4)

4. The transgenic mammal of claim 1 wherein said biologically active peptide is selected from the group consisting of erythropoietin, tissue plasminogen activator and gamma interferon.

CLMS(5)

5. The transgenic mammal of claim 1 wherein said **immunoglobulin**
comprises a tetrameric antibody directed against an enzyme.

CLMS(6)

6. The transgenic mammal of claim 1 wherein said mammal is selected from
the group consisting of mice, cows, sheep, goats, and pigs.

CLMS(7)

7. The transgenic mammal of claim 1 wherein said promoter is selected
from the group consisting of the casein promoter, the beta lactoglobulin
promoter, the whey acid protein promoter, and the **lactalbumin** **promoter**.

CLMS(8)

8. The transgenic mammal of claim 1 wherein said immmunoglobulin comprises heavy and light chains.

CLMS(9)

9. The transgenic mammal of claim 1 wherein said **immunoglobulin** is
of human origin.

CLMS(10)

10. A transgenic non-human goat all of whose germ cells and somatic cells contain a heterologous **immunoglobulin** protein-coding sequence
operatively linked to a promoter sequence that directs the preferential expression of said protein-coding sequence in mammary gland epithelial
cells, thereby providing a heterologous and assembled **immunoglobulin**
in the milk of said goat, wherein said heterologous and assembled **immunoglobulin** is in a functional configuration and is produced at
levels of at least about 1 mg/ml in the milk of said goat.

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L12: 2 of 2

CLAIMS:

CLMS(1)

What is claimed is:

1. A high level expression method for providing a heterologous and assembled **immunoglobulin**, in the milk of a transgenic mammal comprising:
obtaining milk from a transgenic mammal having introduced into its germline a heterologous **immunoglobulin** protein-coding sequence
operatively linked to a promoter sequence that results in the preferential expression of said protein-coding sequence in mammary gland epithelial cells, thereby providing said heterologous and assembled **immunoglobulin** in the milk of said mammal, wherein said
heterologous and assembled **immunoglobulin** is a functional configuration and is produced at level of at least about 1 mg/ml in the milk of said mammal.

CLMS(2)

2. The method of claim 1 wherein said mammal is selected from the group
consisting of mice, sheep, and pigs.

CLMS(3)

3. The method of claim 1 wherein said promoter is selected from the group consisting of the beta lactoglobulin promoter, whey acid protein promoter, and the **lactalbumin** **promoter**.

CLMS(4)

4. The method of claim 1 wherein said **immunoglobulin** comprises heavy
and light chains.

CLMS(5)

5. The method of claim 1 wherein said **immunoglobulin** is of human
origin.

CLMS(6)

6. The method of claim 1 wherein said **immunoglobulin** is purified
from the milk of said mammal.

CLMS(7)

7. The method of claim 1 wherein said promoter is the casein promoter.

CLMS(8)

8. A high level expression method for providing a heterologous and assembled **immunoglobulin**, in the milk of a transgenic goat comprising:
obtaining milk from a transgenic goat having introduced into its germline a heterologous **immunoglobulin** protein-coding sequence
operatively linked to a promoter sequence that results in the preferential expression of said protein-coding sequence in mammary gland epithelial cells, thereby providing said heterologous and assembled **immunoglobulin** in the milk of said goat, wherein said
heterologous and assembled **immunoglobulin** is a functional configuration and is produced at levels of at least about 1 mg/ml in the milk of said goat.

CLMS(9)

9. The method of claim 8 wherein said promoter is selected from the group consisting of the beta lactoglobulin promoter, whey acid protein promoter, and the **lactalbumin** **promoter**.

CLMS(10)

10. The method of claim 8 wherein said **immunoglobulin** comprises
heavy and light chains.

CLMS(11)

11. The method of claim 8 wherein said **immunoglobulin** is of human
origin.

CLMS(12)

12. The method of claim 8 wherein said **immunoglobulin** is purified
from the milk of said goat.

CLMS(13)

13. The method of claim 8 wherein said promoter is the casein promoter.

=> s 536/23.1/ccls

L13 2866 536/23.1/CCLS

=> s 536/23.5/ccls

L14 2126 536/23.5/CCLS

=> s 536/23.53/ccls

L15 192 536/23.53/CCLS

=> s 536/24.1/ccls

L16 1349 536/24.1/CCLS

=> 514/44/ccls

'514' IS NOT A RECOGNIZED COMMAND

=> s 514/44/ccls

L17 733 514/44/CCLS

=> s 435/320.1/ccls

L18 6152 435/320.1/CCLS

=> s l13-l18

L19 8837 (L13 OR L14 OR L15 OR L16 OR L17 OR L18)

=> s l19 and l1

L20 2207 L19 AND L1

=> s l20 and (whey acidic protein or casein or lactoglobulin or lactalbumin)

4328 WHEY
98021 ACIDIC
73025 PROTEIN
45 WHEY ACIDIC PROTEIN
(WHEY(W)ACIDIC(W)PROTEIN)
17607 CASEIN
635 LACTOGLOBULIN
1127 LACTALBUMIN
L21 295 L20 AND (WHEY ACIDIC PROTEIN OR CASEIN OR LACTOGLOBULIN OR
LAC
TALBUMIN)

=> s l20 and (whey acidic protein or casein or lactoglobulin or lactalbumin)(w)(promoter#)

4328 WHEY
98021 ACIDIC
73025 PROTEIN
45 WHEY ACIDIC PROTEIN
(WHEY(W)ACIDIC(W)PROTEIN)
17607 CASEIN
635 LACTOGLOBULIN
1127 LACTALBUMIN
36024 PROMOTER#
47 (WHEY ACIDIC PROTEIN OR CASEIN OR LACTOGLOBULIN OR LACTALBU
MIN
)(W)(PROMOTER#)
L22 12 L20 AND (WHEY ACIDIC PROTEIN OR CASEIN OR LACTOGLOBULIN OR
LAC
TALBUMIN)(W)(PROMOTER#)

=> d l- cit ab

1. 5,928,904, Jul. 27, 1999, DNA encoding recombinant IL4 antibodies
useful in treatment of IL4 mediated disorders; Stephen D. Holmes, et al.,
435/69.6, 70.21, 71.1, **320.1**, 326, 328, 335; 530/300, 350, 387.3, 388.23; **536/23.5**, **23.53** [IMAGE AVAILABLE]

US PAT NO: 5,928,904 [IMAGE AVAILABLE] L22: 1 of 12

ABSTRACT:
Chimeric and humanized IL4 MAbs derived from high affinity MAbs, pharmaceutical compositions containing same, and methods of treatment are
provided.

2. 5,877,010, Mar. 2, 1999, Thymidine kinase mutants; Lawrence A. Loeb,
et al., **435/320.1**, 243, 325; 536/23.2, **23.5**, 23.72, **24.1** [IMAGE AVAILABLE]

US PAT NO: 5,877,010 [IMAGE AVAILABLE] L22: 2 of 12

ABSTRACT:
The present invention provides isolated nucleic acid molecules encoding a
Herpesviridae thymidine kinase enzyme comprising one or more mutations,
at least one of the mutations encoding an amino acid substitution upstream from a DRH nucleoside binding site which increases a biological
activity of the thymidine kinase, as compared to unmutated thymidine kinase. Within another aspect, one of the mutations is an amino acid substitution within a DRH nucleoside binding site which increases a biological activity of the thymidine kinase, as compared to unmutated thymidine kinase. Also provided are vectors suitable for expressing such
DNA molecules, as well as methods for utilizing such vectors.

3. 5,736,388, Apr. 7, 1998, Bacteriophage-mediated gene transfer systems
capable of transfecting eukaryotic cells; Sunil Chada, et al., **435/320.1**; 424/93.6; 435/235.1; **514/44** [IMAGE AVAILABLE]

US PAT NO: 5,736,388 [IMAGE AVAILABLE] L22: 3 of 12

ABSTRACT:
Lamboid bacteriophage capable of specifically interacting with and delivering nucleic acid molecules to eukaryotic cells are disclosed. Such
bacteriophage-derived gene transfer systems target one or more specific
receptors on eukaryotic cells, for instance by incorporating mutant tail fiber proteins or by incorporating known ligands for specific eukaryotic receptors into lambda phage. Also disclosed are methods for identifying
and producing modified bacteriophage tail fiber polypeptides capable of
specifically interacting with eukaryotic transmembrane proteins. Methods
of treating diseases using such gene transfer systems are also disclosed.

4. 5,688,677, Nov. 18, 1997, Deoxyribonucleic acids containing inactivated hormone responsive elements; Karl M. Ebert, et al., **536/23.5**, **24.1** [IMAGE AVAILABLE]

US PAT NO: 5,688,677 [IMAGE AVAILABLE] L22: 4 of 12

ABSTRACT:
A DNA comprising at least one inactivated hormone responsive element and
a nucleic acid sequence encoding a membrane-associated protein is described. Therapeutic compositions and cells including the DNA are also
described. Other aspects of the invention include methods of treating subjects having cystic fibrosis which include administering an effective amount of the DNA to subjects having cystic fibrosis such that functional
cystic fibrosis transmembrane conductance regulator is produced by the
subject at a level which is not detrimental to the subject. The present invention also pertains to a method of introducing the DNA into a cell such that the membrane-associated protein is produced at a level which is
not detrimental to the cell and cells produced by this method. Still other aspects of the invention include a method of assaying DNA for the
presence or absence of a hormone responsive element in a species in which
the hormone responsive element is functional and a method of selectively
breeding female transgenic mammals which produce a protein of interest.

5. 5,683,892, Nov. 4, 1997, DNA encoding recombinant IL-5 antagonists
useful in treatment of IL-5 mediated disorders; Robert S. Ames, Jr., et al., 435/69.1, 69.3, 70.21, 252.3, **320.1**, 328; **536/23.53** [IMAGE
AVAILABLE]

US PAT NO: 5,683,892 [IMAGE AVAILABLE] L22: 5 of 12

ABSTRACT:
DNA encoding chimeric, humanized and other IL-5 mAbs, derived from high
affinity neutralizing mAbs, pharmaceutical compositions containing same,
methods of treatment and diagnostics are provided.

6. 5,681,746, Oct. 28, 1997, Retroviral delivery of full length factor VIII; Mordechai Bodner, et al., 435/350, **320.1**, 366, 371; **536/23.5** [IMAGE AVAILABLE]

US PAT NO: 5,681,746 [IMAGE AVAILABLE] L22: 6 of 12

ABSTRACT:
Retroviral vectors for directing expression of full length factor VIII in transduced host cells, plasmids encoding the same, and host cells transformed, transfected, or transduced therewith are disclosed. Also disclosed are retroviral particles comprising such retrovital vectors, as are methods for making such particles in suitable packaging cells. Retroviral particles so produced may be amphotropic, ecotropic, polytropic, or xenotropic; alternatively, they may comprise chimeric or hybrid envelope proteins to alter host range. Also described are retrovital particles comprising retroviral vectors for directing full length factor VIII expression which are complement resistant. Pharmaceutical compositions comprising retrovital particles of the invention are also disclosed, as are methods of treating mammals, particularly humans, afflicted with hemophilia.

7. 5,648,243, Jul. 15, 1997, Human serum albumin expression construct;
David R. Hurwitz, et al., 435/69.6, **320.1**; **536/23.1**, **23.5**,
24.1, 24.2 [IMAGE AVAILABLE]

US PAT NO: 5,648,243 [IMAGE AVAILABLE] L22: 7 of 12

ABSTRACT:
The present invention provides DNA constructs comprising a promoter DNA
sequence and a DNA sequence coding for human serum albumin. In one
embodiment the human serum albumin sequence comprises at least one, but
not all, of the introns in the naturally occurring gene encoding for the HSA protein. In another embodiment the DNA constructs comprise a 5'
regulatory sequence which directs the expression and secretion of HSA protein in the milk of a transgenic animal. Preferably, the promoter gene
is a milk protein promoter sequence such as .beta.-lactoglobulin. The present invention also provides transgenic animals which secrete HSA in
the milk of lactating females. The present invention also provides vectors comprising the constructs of the present invention.

8. 5,476,995, Dec. 19, 1995, Peptide production; Anthony J. Clark, et al., 800/16; 435/69.1, 317.1, **320.1** [IMAGE AVAILABLE]

US PAT NO: 5,476,995 [IMAGE AVAILABLE] L22: 8 of 12

ABSTRACT:
A method of producing a proteinaceous compound, involves incorporating a
DNA sequence coding for polypeptide into a gene of a mammal (such as a
sheep) coding for a milk whey protein in such a way that the DNA sequence
is expressed in the mammary gland of the adult female mammal. The proteinaceous compound may be a (optionally modified) protein such as a
blood coagulation factor. The DNA sequence is preferably inserted into
the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The proteinaceous compound will generally be recovered from milk of the female mammal, but may (for example if it is
an enzyme) be used in situ.

9. 5,366,894, Nov. 22, 1994, Peptide production; Anthony J. Clark, et

al., **435/320.1**, 69.1, 325 [IMAGE AVAILABLE]

US PAT NO: 5,366,894 [IMAGE AVAILABLE] L22: 9 of 12

ABSTRACT:
A method of producing a substance comprising a peptide, involves incorporating a DNA sequence coding for the peptide into a gene of a mammal (such as a sheep) coding for a milk whey protein in such a way
that the DNA sequence is expressed in the mammary gland of the adult
female mammal. The substance may be an (optionally modified) protein such
as a blood coagulation factor. The DNA sequence is preferably inserted
into the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The substance will generally be recovered from milk
of the female mammal, but may (for example if it is an enzyme) be used in
situ.

10. 5,322,775, Jun. 21, 1994, Peptide production; Anthony J. Clark, et al., 435/69.1, 69.6, 69.7, 317.1, **320.1**; 530/412 [IMAGE AVAILABLE]

US PAT NO: 5,322,775 [IMAGE AVAILABLE] L22: 10 of 12

ABSTRACT:
A method of producing a proteinaceous compound, involves incorporating a
DNA sequence coding for a polypeptide chain of said compound into a gene
of a mammal (such as a sheep) coding for a milk whey protein in such a
way that the DNA sequence is expressed in the mammary gland of the adult
female mammal. The proteinaceous compound may be a (optionally modified)
protein such as a blood coagulation factor. The DNA sequence is preferably inserted into the first exon of a gene coding for a whey protein such as beta-lactoglobulin. The proteinaceous compound will generally be recovered from milk of the female mammal, but may (for example if it is an enzyme) be used in situ.

11. 5,268,275, Dec. 7, 1993, Vitamin K-dependent carboxylase; Darrel W.
Stafford, et al., 435/69.1, 69.6, 232, 252.3, **320.1**, 352, 354, 358, 366; 536/23.2 [IMAGE AVAILABLE]

US PAT NO: 5,268,275 [IMAGE AVAILABLE] L22: 11 of 12

ABSTRACT:
Isolated DNA encoding a vitamin K dependent carboxylase is disclosed. The
carboxylase is selected from the group consisting of: (a) isolated DNA which encodes bovine or human vitamin K dependent carboxylase; (b) isolated DNA which hybridizes to isolated DNA of (a) above and which
encodes a vitamin K dependent carboxylase; and (c) isolated DNA differing
from the isolated DNAs of (a) and (b) above in nucleotide sequence due to
the degeneracy of the genetic code, and which encodes a vitamin K dependent carboxylase. Also disclosed are vectors and host cells containing the aforesaid DNA, methods of using the same, and purified
protein coded for by the aforesaid DNA.

12. 4,873,316, Oct. 10, 1989, Isolation of exogenous recombinant proteins from the milk of transgenic mammals; Harry Meade, et al., 800/7;
435/69.1, 69.2, 69.4, 69.5, 69.6, 69.8; 530/360, 361, 416, 417, 418, 832,
833; **536/23.1**, 23.4, **23.5**; 800/18 [IMAGE AVAILABLE]

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L22: 12 of 12

ABSTRACT:
This invention relates to the production of recombinant proteins in mammals' milk. Particularly, this invention relates to an expression system comprising the mammal's **casein** **promoter** which when
transgenically incorporated into a mammal permits the female species of
that mammal to produce the desired recombinant protein in or along with
its milk. This invention also relates to the transgenic mammal that produces the desired recombinant product in its milk.

=> d 12 kwic

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L22: 12 of 12
US-CL-CURRENT: 800/7; 435/69.1, 69.2, 69.4, 69.5, 69.6, 69.8; 530/360,
361, 416, 417, 418, 832, 833; **536/23.1**, 23.4, **23.5**; 800/18

ABSTRACT:
This . . . to the production of recombinant proteins in mammals' milk.
Particularly, this invention relates to an expression system comprising the mammal's **casein** **promoter** which when transgenically incorporated into a mammal permits the female species of that mammal to
produce the desired recombinant protein. . .

DETDESC:

DETD(8)

Among the milk-specific protein promoters useful in the various embodiments of this invention are the **casein** **promoters** and the
beta **lactoglobulin** **promoter**. The **casein** **promoters** may,
for example, be selected from an alpha **casein** **promoter**, a beta
casein **promoter** or a kappa **casein** **promoter**. Preferably,
the **casein** **promoter** is of bovine origin and is an alpha S-1 **casein** **promoter**. Among the promoters that are specifically activated in mammary tissue and are thus useful in accordance with this
invention is. . .

DETDESC:

DETD(10)

Among . . . antitrypsin, animal growth hormones, Mullerian Inhibiting
Substance (MIS), cell surface proteins, insulin, interferons, interleukins, milk lipases, antiviral proteins, peptide hormones, **immunoglobulins**, lipocortins and other recombinant protein products.

CLAIMS:

CLMS(1)

We . . .

recombinate protein comprising the steps of:
a. producing milk in a transgenic mammal characterized by an expression
system comprising a **casein** **promoter** operatively linked to an
exogenous DNA sequence coding for the recombinant protein through a DNA
sequence coding for a signal. . .

=> d 12 fro

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L22: 12 of 12
DATE ISSUED: Oct. 10, 1989
TITLE: Isolation of exogenous recombinant proteins from the milk
of transgenic mammals
INVENTOR: Harry Meade, Newton, MA
Nils Lonberg, New York, NY
ASSIGNEE: Biogen, Inc., Cambridge, MA (U.S. corp.)

APPL-NO: 07/065,994
DATE FILED: Jun. 23, 1987
INT-CL: [4] C07K 3/02; C07K 3/12; C07K 3/18; C12N 15/00
US-CL-ISSUED: 530/412, 360, 361, 833, 832, 416, 417, 418; 435/68, 172.1,
172.3, 240.2; 935/53, 55, 70, 111; 800/1; 536/27, 28, 29
US-CL-CURRENT: 800/7; 435/69.1, 69.2, 69.4, 69.5, 69.6, 69.8; 530/360,
361, 416, 417, 418, 832, 833; **536/23.1**, 23.4, **23.5**; 800/18
SEARCH-FLD: 435/68, 172.1, 172.3, 226, 240.2; 530/832, 833, 412, 360,
361, 303; 800/1; 935/53, 55, 70; 536/27, 28, 29
REF-CITED:

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4,736,866	4/1988	Leder et al.	

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1299-303, May 1987).
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ART-UNIT: 186
PRIM-EXMR: Margaret Moskowitz
ASST-EXMR: Jeff P. Kushan
LEGAL-REP: James F. Haley, Jr., Teresa L. Solomon

ABSTRACT:
This invention relates to the production of recombinant proteins in mammals' milk. Particularly, this invention relates to an expression system comprising the mammal's **casein** **promoter** which when
transgenically incorporated into a mammal permits the female species of
that mammal to produce the desired recombinant protein in or along with
its milk. This invention also relates to the transgenic mammal that produces the desired recombinant product in its milk.
3 Claims, 1 Drawing Figures

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 *  JAPANESE PATENT ABSTRACTS   *
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 * THE FILE IS CURRENT THROUGH MARCH 31, 1999.
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IRD CNOABS

=> s l1

L23 505 IMMUNOGLOB?

=> s l2

```
      505 IMMUNOGLOB?
      580 WHEY
    14269 ACIDIC
    10862 PROTEIN
        0 WHEY ACIDIC PROTEIN
          (WHEY(W)ACIDIC(W)PROTEIN)
L24     0 L1 AND WHEY ACIDIC PROTEIN
```

=> s l3

```
      505 IMMUNOGLOB?
      580 WHEY
    14269 ACIDIC
    10862 PROTEIN
        0 WHEY ACIDIC PROTEIN
          (WHEY(W)ACIDIC(W)PROTEIN)
     2534 PROMOTER#
L25     0 L2 AND PROMOTER#
```

=> s l4

```
      505 IMMUNOGLOB?
      580 WHEY
    14269 ACIDIC
    10862 PROTEIN
        0 WHEY ACIDIC PROTEIN
          (WHEY(W)ACIDIC(W)PROTEIN)
     2534 PROMOTER#
     7370 CONSTRUCT#
    15691 VECTOR#
     2014 PLASMID#
L26     0 L3 AND (CONSTRUCT# OR VECTOR# OR PLASMID#)
```

=> s l5

```
      505 IMMUNOGLOB?
     1448 CASEIN
L27     4 IMMUNOGLOB? AND CASEIN
```

=> d l- cit ab

1. 07-285885, Oct. 31, 1995, PRODUCTION OF **IMMUNOGLOBULIN**; HIFUMI OISHI, et al., A61K 39/395; B01D 61/14; C07K 16/06

07-285885 L27: 1 of 4

ABSTRACT:

PURPOSE: To provide **immunoglobulin** and a method for producing an **immunoglobulin** monomer from the resultant **immunoglobulin** (antigen).

CONSTITUTION: **Casein** is subjected to an isoelectric point (pH4.5 to 4.6) precipitation treatment or treated with an enzyme such as rennin to obtain whey. Ethylenediaminetetraacetic acid or glycine is added to the whey so that the concentration of the respective components may be 0.5 to 10mM or 50 to 500mM. pH of the whey is adjusted to 6.0 to 6.5 by using a sodium citrate solution and a cation-exchange resin is brought into contact therewith. The treated material is further treated by using an ultrafiltration module having 50000 or 100000 dalton separation limitation, thus obtaining the objective **immunoglobulin**.

2. 63-135336, Jun. 7, 1988, DRUG FOR INTESTINAL DISORDER; TOSHIRO HORI,

et al., A61K 39/395; A61K 35/20

63-135336 L27: 2 of 4

ABSTRACT:

PURPOSE:To obtain an agent for controlling intestinal disorder, by compounding **immunoglobulin** of cattle whey as an active component.

CONSTITUTION:The objective intestinal disorder controlling agent can be
produced by using **immunoglobulin** of cattle whey (whole **immunoglobulin** existing in cattle whey) in an amount of .gtoreq.50%
of the whole solid component and properly mixing the **immunoglobulin**
with a vehicle. It is necessary to administer the **immunoglobulin** of
cattle whey at a dose of .gtoreq.10mg/kg and the dose is preferably .ltoreq.1g for person taking the easiness of administration into consideration. The **immunoglobulin** of cattle whey used in the agent
can be produced by treating normal milk of healthy cow with an enzyme
and/or acid, removing precipitated **casein**, subjecting the obtained whey part to ion-exchange treatment, etc., to remove low-molecular weight
soluble salts, lactose, etc., and separating and concentrating the **immunoglobulin** fraction. The **immunoglobulin** may be used in the
form of powder, liquid, etc., however, use of pulverized globulin is preferable for the convenience of storage and handling.

3. 63-135323, Jun. 7, 1988, COSMETIC; TOSHIRO HORI, et al., A61K 7/40

63-135323 L27: 3 of 4

ABSTRACT:

PURPOSE:To obtain a cosmetic suitably useful for treating pimples, by
blending a cosmetic base with **immunoglobulin** of bovine milk serum as
an active ingredient.

CONSTITUTION:Bovine milk serum part obtained by treating ordinary milk
or healthy bovine with an enzyme and/or acid, removing precipitating **casein** form the milk is subjected to ion exchange, gel filtration, affinity chromatography or ultrafiltration with 100,000mol.wt. of elimination limit to remove low-molecular soluble salt, lactose, protein
having tens thousands molecular weight, etc. The prepared **immunoglobulin** fraction is separated and concentrated to give **immunoglobulin** of bovine milk serum. A cosmetic is blended with the
immunoglobulin as an active ingredient. The amount of the **immunoglobulin** in the cosmetic is preferably .gtoreq.5wt% calculated
as a solid substance.

4. 60-75433, Apr. 27, 1985, METHOD FOR CONCENTRATING **IMMUNOGLOBULIN**
IN COW'SCOLOSTRUM; YOSHIYUKI MINAMI, et al., A61K 39/395

60-75433 L27: 4 of 4

ABSTRACT:

PURPOSE:To concentrate efficiently the titled globulin, by defatting cow's colostrum, adding an acid to the defatted cow's colostrum to adjust
the pH to a specific value, adding pepsin or rennin thereto to coagulate and separate **casein**, and ultrafiltering the resultant whey.

CONSTITUTION:A colostrum collected within about one week after the
delivery of a cow is defatted with a cream separator, and an acid, e.g. acetic or propionic acid, is added to the defatted colostrum to adjust the pH to 5.0.approx.6.0. Pepsin or rennin is then added thereto coagulate **casein**. In the process, the defatted colostrum is preferably heated to 50.approx.55.degrees C.. Crud is flocculated by heating, and whey is collected. The recovered whey is then contrifuged at
a low speed, and the remaining fine particles are removed. The whey is
then preferably quenched to 10.degrees C. or below. The resultant whey is
concentrated in an ultrafiltration apparatus, e.g. plate form, etc. The resultant whey containing concentrated **immunoglobulin** is freeze-dried
or spray-dried to give a raw material used to prepare a feed for young animals.

```
=> s l9

        505 IMMUNOGLOB?
         30 LACTOGLOBULIN
L28       0 IMMUNOGLOB? AND LACTOGLOBULIN

=> s l11

        505 IMMUNOGLOB?
         39 LACTALBUMIN
L29       0 L1 AND LACTALBUMIN

=> file epoab

FILE 'EPOABS' ENTERED AT 17:44:16 ON 04 AUG 1999

 ********************************
 *  EUROPEAN PATENT ABSTRACTS   *
 ********************************


   FILE 'EPOABS' ENTERED AT 17:44:16 ON 04 AUG 1999

=> s l23

L30       894 IMMUNOGLOB?

=> s l24

        894 IMMUNOGLOB?
        852 WHEY
       7450 ACIDIC
      12508 PROTEIN
          3 WHEY ACIDIC PROTEIN
            (WHEY(W)ACIDIC(W)PROTEIN)
L31       0 L1 AND WHEY ACIDIC PROTEIN

=> s l26

        894 IMMUNOGLOB?
        852 WHEY
       7450 ACIDIC
      12508 PROTEIN
          3 WHEY ACIDIC PROTEIN
            (WHEY(W)ACIDIC(W)PROTEIN)
       3960 PROMOTER#
       2822 CONSTRUCT#
       9024 VECTOR#
       1640 PLASMID#
L32       0 L3 AND (CONSTRUCT# OR VECTOR# OR
PLASMID#)

=> s l27

        894 IMMUNOGLOB?
        510 CASEIN
L33       5 IMMUNOGLOB? AND CASEIN

=> d 1- cit ab


1. US 05487975A, Jan. 30, 1996, Biotin/avidin formulation; PHILLIP
C
MILLER, et al., G01N 33/535

US 05487975A                    L33: 1 of 5

ABSTRACT:
```

<CHG DATE=19960327 STATUS=O>The present invention provides an improved
biotin-avidin formulation in which a biotinylated antibody conjugate or an avidin-enzyme conjugate is present in a suitable diluent for immunohistochemical staining. The diluent additionally comprises **casein** in an amount sufficient to prevent charge interactions of the
conjugate with a tissue section and gamma globulin in an amount sufficient to prevent Fc receptor binding and any hydrophobic interaction
of the conjugate with a tissue section. In a preferred embodiment, the **immunoglobulin** is from the same species as the biotinylated antibody
conjugate. The formulation effectively reduces overall unwanted binding,
irrespective of the source of the binding.

2. WO 09508562A1, Mar. 30, 1995, METHOD OF OBTAINING **IMMUNOGLOBULINS** FROM COLOSTRUM AND THEIR USE IN PHARMACEUTICAL COMPOSITION; CONOR JOHN GRAHAM, C07K 1/14; C07K 1/30; C07K 16/04; A61K 9/20; A61K 9/30; A61K 39/395

WO 09508562A1 L33: 2 of 5

ABSTRACT:

A method of obtaining a high purity **immunoglobulin** preparation from
an antibody rich colostrum which includes: (i) removing milk fat from the
colostrum to obtain a low-fat colostrum; (ii) pasteurising the low-fat colostrum; (iii) coagulating the pasteurised, low-fat colostrum and removing milk curd containing **casein**; (iv) centrifuging remaining
liquid to remove percipitates; (v) removing lactose, minerals and water to obtain an antibody containing fraction; (vi) dissolving the antibody containing fraction in THRESH buffer and idolizing against the same buffer; and (vii) concentrating the antibody containing solution to obtain a 10 % by weight antibody solution. A pharmaceutical composition
including a core element which includes an active antibody component derived by the above method, wherein the core element is in the form of a
tablet, and wherein the compression forces used to prepare the tablet are
such that they do not injure or denature the active antibodies.

3. WO 08910139A1, Nov. 2, 1989, PREPARATION WITH ANTIBODY ACTIVITY AND BROAD SPECTRUM; HERBERT DICHTELMUELLER, et al., A61K 39/395; //C07K 15/06; C07K 3/02

WO 08910139A1 L33: 3 of 5

ABSTRACT:

<CHG DATE=19940730 STATUS=O>A preparation with antibody activity is
prepared from colostrum of non-immunized mammals extracted during the
first 30 hours, preferably however during the first 10 hours, following parturition. The colostrum is diluted with water, pasteurized, and after removal of the **casein** and fat, concentrated and stabilized. The preparation has a high **immunoglobulin** content (>80 %) and low
anticomplementary activity. It can be administered orally in humans and
intravenously in veterinary medicine. It can be used successfully, alone or in combination with other pharmaceutical substances, to treat bacteria- or toxin-induced diseases, in particular severe diarrhea in AIDS patients and other immunological disorders, travellers' diarrhea and
toxin-induced infantile diarrhea, gastric and intestinal ulcers, as well as chronic and acute Yersinia infections, and to combat protozoa.

4. GB 02188526A, Oct. 7, 1987, Whey protein; JOHN BURTON, et al., A23C 9/146; A23J 1/20

GB 02188526A L33: 4 of 5

ABSTRACT:

    A proteinaceous material obtained from milk or
casein-containing milk products, or an analogue or derivative thereof, comprises a polypeptide or mixture of polypeptides substantially
free of native alpha-, beta- and kappa-**casein**, serum albumin, alpha-lactalbumin, beta-lactoglobulin and the **immunoglobulins**, and
  i) remains in solution at pH 4.6 to pH 5.3 at 20 DEG C;
  ii) is anionic at pH 4.6 to pH 5.3; and   iii)
forms a gel when an aqueous solution containing at least 12% w/v of the
proteinaceous material at 20 DEG C and pH 4,5 or below is allowed to stand for 18 to 24 h. <??>Milk whey at pH 4 to 6 may be contacted
with an anion exchange resin, the resin may be eluted with HCl or NaCl
and the product may be concentrated by ultrafiltration or thermal evaporation and/or spray dried or freeze-dried.

5. GB 02179947A, Mar. 18, 1987, Process for the extraction of proteins from milk; PIERRE FREDERIC EMMANUE MONSAN, et al., C07K 3/22; C07K 3/02; C07K 3/28

GB 02179947A L33: 5 of 5

ABSTRACT:

    A process for the extraction of proteins,
preferably lacto-transferrins or **IMMUNOGLOBULINS**, from milk from
which the **casein** and the fatty substances have been substantially removed, comprises adsorbing the proteins on an ion exchanger followed by
elution whereby the desired protein fraction is obtained, the adsorption and the elution being carried out at substantially the same pH, preferably 5 to 8.5, especially 7 to 8. <??>The **casein**-free milk is preferably concentrated about five times, by ultrafiltration, before adsorption.

=> s l28

894 IMMUNOGLOB?
40 LACTOGLOBULIN
L34 3 IMMUNOGLOB? AND LACTOGLOBULIN

=> d 1- cit ab

1. US 04849241A, Jul. 18, 1989, Novel process for lowering the concentration of beta -**lactoglobulin** in cheese whey; SHALAN A AL-MASHIKI, et al., A23C 21/10

US 04849241A L34: 1 of 3

ABSTRACT:

<CHG DATE=19940730 STATUS=O>A process for lowering the concentration of
beta -**lactoglobulin** in cheese whey while retaining the **immunoglobulins** in said cheese whey which comprises treating said
cheese whey with a polyphosphate, such as sodium hexametaphosphate,
within a pH range of from about 3.8 to about 4.7.

2. US 04112123A, Sep. 5, 1978, Nutritionally balanced single food composition and method of production; WILLARD LEWIS ROBERTS, A23C 21/00

US 04112123A L34: 2 of 3

ABSTRACT:

<CHG DATE=19940730 STATUS=O>There is provided a single nutritionally
balanced food composition for oral ingestion and producing low residues
and diminished stoolings for use with patients having abnormal catabolic
states. The composition comprises a water soluble or suspendible, essentially undenatured protein obtained from the ultra-filtration of whey and containing beta **lactoglobulin**, alphalactalbumin, **immunoglobulins**, and serum albumin; and medium-chain triglycerides of
predominately 6 to 10 carbon atoms in the fatty acid chain. The composition will also include digestable carbohydrates, e.g. dextrose, sucrose, corn syrup solids, etc., and a food grade emulsifier. The composition can provide up to three calories per cubic centimeter of solution that can be drip fed and has a low osmolarity. The composition
has a Protein Efficiency Ratio (PER) which is at least 3.1 and more usually 3.2. The protein is essentially bland to the taste and the composition therefore may be flavored as desired. The composition may be
provided in a dried or reconstituted form of either low viscosity for tube-feeding and sipping or high viscosities for simulated foods, e.g. custards, puddings, candies, fillings for sandwich cookies, et cetera.

3. GB 02188526A, Oct. 7, 1987, Whey protein; JOHN BURTON, et al., A23C
9/146; A23J 1/20

GB 02188526A L34: 3 of 3

ABSTRACT:

    A proteinaceous material obtained from milk or
casein-containing milk products, or an analogue or derivative thereof, comprises a polypeptide or mixture of polypeptides substantially free of
native alpha-, beta- and kappa-casein, serum albumin, alpha-lactalbumin,
beta-**lactoglobulin** and the **immunoglobulins**, and   i)
remains in solution at pH 4.6 to pH 5.3 at 20 DEG C;   ii) is
anionic at pH 4.6 to pH 5.3; and   iii) forms a gel when an
aqueous solution containing at least 12% w/v of the proteinaceous material at 20 DEG C and pH 4,5 or below is allowed to stand for 18 to 24
h. <??>Milk whey at pH 4 to 6 may be contacted with an anion exchange resin, the resin may be eluted with HCl or NaCl and the product
may be concentrated by ultrafiltration or thermal evaporation and/or spray dried or freeze-dried.

=> s l29

894 IMMUNOGLOB?
49 LACTALBUMIN
L35 1 L1 AND LACTALBUMIN

=> d cit ab

1. GB 02188526A, Oct. 7, 1987, Whey protein; JOHN BURTON, et al., A23C
9/146; A23J 1/20

GB 02188526A L35: 1 of 1

ABSTRACT:

    A proteinaceous material obtained from milk or
casein-containing milk products, or an analogue or derivative thereof, comprises a polypeptide or mixture of polypeptides substantially free of
native alpha-, beta- and kappa-casein, serum albumin, alpha-**lactalbumin**, beta-lactoglobulin and the **immunoglobulins**,
and   i) remains in solution at pH 4.6 to pH 5.3 at 20 DEG
C;   ii) is anionic at pH 4.6 to pH 5.3; and   iii)
forms a gel when an aqueous solution containing at least 12% w/v of the
proteinaceous material at 20 DEG C and pH 4,5 or below is allowed to stand for 18 to 24 h. <??>Milk whey at pH 4 to 6 may be contacted
with an anion exchange resin, the resin may be eluted with HCl or NaCl
and the product may be concentrated by ultrafiltration or thermal evaporation and/or spray dried or freeze-dried.

=> file uspat

FILE 'USPAT' ENTERED AT 17:47:12 ON 04 AUG 1999

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 ********************************
 *    U.S. PATENT TEXT FILE     *
 *                              *
 * THE WEEKLY PATENT TEXT AND IMAGE DATA IS CURRENT *
 * THROUGH AUGUST 3,1999        *
 *                              *
 *                              *
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=> d his

(FILE 'USPAT' ENTERED AT 17:22:03 ON 04 AUG 1999)
L1 11569 S IMMUNOGLOB?
L2 18 S L1 AND WHEY ACIDIC PROTEIN
L3 16 S L2 AND PROMOTER#
L4 16 S L3 AND (CONSTRUCT# OR VECTOR# OR PLASMID#)
L5 908 S IMMUNOGLOB? AND CASEIN
L6 410 S L5 AND PROMOTER#
L7 387 S L6 AND (CONSTRUCT# OR VECTOR# OR PLASMID#)
L8 20 S IMMUNOGLOB? AND CASEIN PROMOTER
L9 208 S IMMUNOGLOB? AND LACTOGLOBULIN
L10 8 S IMMUNOGLOB? AND LACTOGLOBULIN PROMOTER
L11 249 S L1 AND LACTALBUMIN
L12 2 S L1 AND LACTALBUMIN PROMOTER#
L13 2866 S 536/23.1/CCLS
L14 2126 S 536/23.5/CCLS
L15 192 S 536/23.53/CCLS
L16 1349 S 536/24.1/CCLS
L17 733 S 514/44/CCLS
L18 6152 S 435/320.1/CCLS
L19 8837 S L13-L18
L20 2207 S L19 AND L1
L21 295 S L20 AND (WHEY ACIDIC PROTEIN OR CASEIN OR LACTOGLOBULIN
OR
L22 12 S L20 AND (WHEY ACIDIC PROTEIN OR CASEIN OR LACTOGLOBULIN
OR

FILE 'JPOABS' ENTERED AT 17:42:26 ON 04 AUG 1999
L23 505 S L1
L24 0 S L2
L25 0 S L3
L26 0 S L4
L27 4 S L5
L28 0 S L9
L29 0 S L11

FILE 'EPOABS' ENTERED AT 17:44:16 ON 04 AUG 1999
L30 894 S L23
L31 0 S L24
L32 0 S L26
L33 5 S L27
L34 3 S L28
L35 1 S L29

FILE 'USPAT' ENTERED AT 17:47:12 ON 04 AUG 1999

=> log y

U.S. Patent & Trademark Office LOGOFF AT 17:48:09 ON 04 AUG 1999

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**********STN Columbus **********
**

FILE 'HOME' ENTERED AT 10:20:31 ON 10 AUG 1999

=> file medline

COST IN U.S. DOLLARS                SINCE FILE     TOTAL
                                    ENTRY  SESSION
FULL ESTIMATED COST                   0.15     0.15

FILE 'MEDLINE' ENTERED AT 10:20:36 ON 10 AUG 1999

 FILE LAST UPDATED: 6 AUG 1999 (19990806/UP). FILE
COVERS 1960 TO DATE.

 MEDLINE has been reloaded to reflect the annual MeSH changes
made by
 the National Library of Medicine for 1999. Enter HELP RLOAD for
details.

 OLDMEDLINE, data from 1960 through 1965 from the Cumulated
Index
 Medicus (CIM), has been added to MEDLINE. See HELP
CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in
the
 Basic Index. See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY
AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> s immunoglob? or antibod?/ab,bi

'AB' IS NOT A VALID FIELD CODE
      108967 IMMUNOGLOB?
           0 ANTIBOD?/AB
      532337 ANTIBOD?/BI
L1    583923 IMMUNOGLOB? OR ANTIBOD?/AB,BI

=> s l1(5a)(construct# or plasmid# or vector#)/ab,bi

'AB' IS NOT A VALID FIELD CODE
           0 CONSTRUCT#/AB
       26368 CONSTRUCT#/BI
           0 PLASMID#/AB
       71642 PLASMID#/BI
           0 VECTOR#/AB
       59945 VECTOR#/BI
L2       843 L1(5A)(CONSTRUCT# OR PLASMID# OR
VECTOR#)/AB,BI

=> s l2(5)(milk)/ab,bi

MISSING OPERATOR 'L2(5'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l2(5a)(milk)/ab,bi

'AB' IS NOT A VALID FIELD CODE
           0 (MILK)/AB
       48429 (MILK)/BI
L3         2 L2(5A)(MILK)/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS -
CONTINUE? Y/(N):y


L3  ANSWER 1 OF 2  MEDLINE
AN  93078105    MEDLINE
DN  93078105
TI  Concentration of  ***milk***  secretory
***immunoglobulin***  A
    against Shigella virulence  ***plasmid***  -associated antigens as
a
    predictor of symptom status in Shigella-infected breast-fed infants.
AU  Hayani K C; Guerrero M L; Morrow A L; Gomez H F; Winsor D
K; Ruiz-Palacios
    G M; Cleary T G
CS  Department of Pediatrics, University of Texas Medical School,
Houston
    77030.
NC  5-PO1-HD-13021 (NICHD)
SO  JOURNAL OF PEDIATRICS, (1992 Dec) 121 (6) 852-6.
    Journal code: JLZ. ISSN: 0022-3476.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Abridged Index Medicus Journals; Priority Journals; Cancer
Journals
EM  199303
AB  We conducted a prospective, community-based study of healthy
breast-fed
    Mexican infants to determine the protective effects of anti-Shigella
    secretory IgA antibodies in milk. Milk samples were collected
monthly, and
    stool culture specimens were obtained weekly and at the time of
episodes
    of diarrhea. Nineteen breast-fed infants were found to have Shigella
    flexneri, Shigella boydii, or Shigella sonnei in stool samples. Ages
of
    the 10 infants with symptomatic infection and the nine with
asymptomatic
    infection did not differ significantly. Milk samples collected up to
12
    weeks before infection were evaluated by enzyme-linked
immunosorbent assay
    for secretory IgA antibodies against lipopolysaccharides of S.
flexneri,
    S. boydii serotype 2, S. sonnei, and virulence plasmid-associated
    antigens. The geometric mean titers of anti-Shigella
***antibodies***
    to virulence  ***plasmid***  -associated antigens in  ***milk***

    received before infection were eightfold higher in infants who
remained
    well than in those in whom diarrhea developed. The significance of
milk
    secretory IgA directed against lipopolysaccharide was less clear.
We
    conclude that human milk protects infants against symptomatic
shigella
    infection when it contains high concentrations of secretory IgA
against
    virulence plasmid-associated antigens.

L3  ANSWER 2 OF 2  MEDLINE
AN  91093893    MEDLINE
DN  91093893
TI  Human  ***milk***  secretory  ***immunoglobulin***  A to
Shigella
    virulence  ***plasmid***  -coded antigens.
AU  Cleary T G; West M S; Ruiz-Palacios G; Winsor D K; Calva J J;
Guerrero M
    L; Van R
CS  Department of Pediatrics and Microbiology, University of Texas
Medical
    School at Houston 77030..
NC  5-PO1-HD-13021 (NICHD)
SO  JOURNAL OF PEDIATRICS, (1991 Jan) 118 (1) 34-8.
    Journal code: JLZ. ISSN: 0022-3476.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Abridged Index Medicus Journals; Priority Journals; Cancer
Journals
EM  199104
AB  Although antibodies to the lipopolysaccharide antigens of
Shigella have
    been demonstrated in human milk, such antibodies do not explain
the
    putative protective effect of breast-feeding against symptomatic
Shigella
    infection. Shigella species do not share related lipopolysaccharides,
but
    they do possess closely related virulence plasmids that code for the
    proteins essential for cell invasion. We therefore sought to
determine the
    frequency, amount, and duration of excretion of human
***milk***
     ***antibodies***  to these shared virulence  ***plasmid***
-associated
    antigens in populations of different rates of Shigella infection
frequency
    (Mexico City, high; Houston, low). Such antibodies were present in
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the
milk of virtually all the Mexican women but also were present in a large
proportion of milk samples from the women living in Houston. The amounts
of these antibodies were highest in colostrum but after 2 weeks of
lactation fell to stable levels. The frequency and persistence of these
antibodies in the milk of the women from Houston suggest that the memory
and drive for secretion of these antibodies is extremely long lived.

=> s l1(5a)(mammary)

36573 MAMMARY
L4 357 L1(5A)(MAMMARY)

=> s l4(10a)(recombinant)

143021 RECOMBINANT
L5 0 L4(10A)(RECOMBINANT)

=> s l1(5a)(mammary)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 (MAMMARY)/AB
36573 (MAMMARY)/BI
L6 357 L1(5A)(MAMMARY)/AB,BI

=> s l6(5a)(recombinant)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 (RECOMBINANT)/AB
143021 (RECOMBINANT)/BI
L7 0 L6(5A)(RECOMBINANT)/AB,BI

=> s l6(5a)(specific)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 (SPECIFIC)/AB
601385 (SPECIFIC)/BI
L8 33 L6(5A)(SPECIFIC)/AB,BI

=> s l8 and promoter#/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 PROMOTER#/AB
66697 PROMOTER#/BI
L9 0 L8 AND PROMOTER#/AB,BI

=> s l2(5a)(recombin?)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 (RECOMBIN?)/AB
174143 (RECOMBIN?)/BI
L10 57 L2(5A)(RECOMBIN?)/AB,BI

=> s l10(5a)(milk or mammary)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 MILK/AB
48429 MILK/BI
0 MAMMARY/AB
36573 MAMMARY/BI
L11 0 L10(5A)(MILK OR MAMMARY)/AB,BI

=> s l10(10a)(function? or assembl?)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 FUNCTION?/AB
838844 FUNCTION?/BI
0 ASSEMBL?/AB
34637 ASSEMBL?/BI
L12 2 L10(10A)(FUNCTION? OR ASSEMBL?)/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L12 ANSWER 1 OF 2 MEDLINE
AN 1998455662 MEDLINE
DN 98455662
TI Isolation and recombinant expression of an MHV-JHM neutralising monoclonal
antibody.
AU Kolb A F; Lechermaier M; Heister A; Toksoy A; Siddell S G
CS Institute of Virology and Immunology, University of Wurzburg, Germany.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 440 657-64.
Journal code: 2LU. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
EW 19990303
AB The monoclonal antibody A1 (mab A1) efficiently neutralises the infection
of susceptible cells by the murine hepatitis virus MHV-JHM in vitro and in
vivo (Wege et al., 1984). The variable regions of mab A1 were amplified
from mRNA of the respective hybridoma cell line by RT-PCR and integrated
into different eukaryotic expression vectors. The biological
function of the ***recombinant*** ***antibody***
constructs was verified by virus neutralisation assays. Whereas a
complete recombinant antibody (mab A1rec.) expressed in transfected murine
myeloma cells inhibited the MHV-JHM infection as well as the parental
antibody, a single-chain Fv derived from mab A1 did not show any
neutralising activity.

L12 ANSWER 2 OF 2 MEDLINE
AN 97041563 MEDLINE
DN 97041563
TI Lung cancer-reacting human recombinant antibody AE6F4: potential
usefulness in the sputum cytodiagnosis.
AU Shoji M; Kawamoto S; Seki K; Teruya K; Setoguchi Y; Mochizuki K; Kato M;
Hashizume S; Hanagiri T; Yoshimatsu T; Nakanishi K; Yasumoto K; Nagashima
A; Nakahashi H; Suzuki T; Imai T; Shirahata S; Nomoto K; Murakami H
CS Morinaga Institute of Biological Science, Yokohama, Japan.
SO HUMAN ANTIBODIES AND HYBRIDOMAS, (1996) 7 (1) 27-36.
Journal code: A6A. ISSN: 0956-960X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
EW 19970601
AB Human monoclonal antibody (hMAb) AE6F4 has been shown to be potentially
useful for immunocytological detection of lung cancer cells in sputum. By
recombinant DNA technology, IgM type hMAb AE6F4 was switched to IgG. The
IgG mimic ***recombinant*** AE6F4 ***antibody*** expression
plasmid was ***assembled*** using the ***antibody*** heavy
chain gene, which ligated the gene encoding VH and CH1(mu) domains of hMAb
AE6F4 heavy chain to the gene encoding CH2(gamma 1) and CH3(gamma 1)
domains of human IgG heavy chain, and the antibody light chain gene of
hMAb AE6F4. The recombinant antibody expressed by baby hamster kidney
(BHK)-21 cells showed molecular size equivalence to IgG, and consisted of
human mu-gamma hybrid heavy and kappa light chains. The immunological
specificity of the recombinant antibody was the same as that of hMAb AE6F4
by immunoblotting analysis to the 14-3-3 protein, the putative antigen of
hMAb AE6F4, and by immunohistochemical and immunocytological analyses
using tissue sections and sputa of lung cancer patients. The

transfected
BHK-21 cells produced the recombinant antibody persistently and the
productivity was greater than 20 times that by human-human hybridoma
producing hMAb AE6F4.

=> s l2(5a)(mammary)(w)(tumor or tumour)/ab,bi

'AB' IS NOT A VALID FIELD CODE
36573 MAMMARY
0 TUMOR/AB
374204 TUMOR/BI
0 TUMOUR/AB
64119 TUMOUR/BI
L13 0 L2(5A)(MAMMARY)(W)(TUMOR OR TUMOUR)/AB,BI

=> s l1(5a)(mammary)(w)(tumor or tumour)/ab,bi

'AB' IS NOT A VALID FIELD CODE
36573 MAMMARY
0 TUMOR/AB
374204 TUMOR/BI
0 TUMOUR/AB
64119 TUMOUR/BI
L14 74 L1(5A)(MAMMARY)(W)(TUMOR OR TUMOUR)/AB,BI

=> s l14(5a)(promoter#)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 (PROMOTER#)/AB
66697 (PROMOTER#)/BI
L15 0 L14(5A)(PROMOTER#)/AB,BI

=> s l14(5a)(virus)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 (VIRUS)/AB
275885 (VIRUS)/BI
L16 42 L14(5A)(VIRUS)/AB,BI

=> s l16 and milk/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 MILK/AB
48429 MILK/BI
L17 2 L16 AND MILK/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L17 ANSWER 1 OF 2 MEDLINE
AN 81061682 MEDLINE
DN 81061682
TI Ubiquity of natural ***antibodies*** to the ***mammary*** ***tumour*** ***virus*** in mice.
AU Bentvelzen P; Brinkhof J
NC NO1 CP43328 (NCI)
SO ARCHIV FUR GESCHWULSTFORSCHUNG, (1980) 50 (3) 193-203.
Journal code: 746. ISSN: 0003-911X.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198103
AB Sera of female and male mice from eleven inbred mouse strains collected at
either 4, 12, 36 or 60 weeks of age were tested for the presence of
natural ***antibodies*** to the murine ***mammary*** ***tumour*** ***virus*** by means of the Sepharose bead
immunofluorescence assay. Antibodies to the virus proved to be ubiquitous,
but pronounced strain differences were found in titer and onset of
antibody production. These differences were related to neither release of
virus in the ***milk*** nor susceptibility to spontaneous mammary
tumour development of a given strain. Immunological specificity of the
observed reactions was concluded from a) the failure to block the reaction
by absorption with fetal calf serum, mouse ***milk*** or sheep
erythrocytes, while absorption with purified virus abolished the
reactivity; b) the lack of reactivity of rat sera with the mouse mammary
tumour virus in this system; c) the negative response of mouse sera with
Sepharose beads coated with ovalbumin; d) the lack of correlation between
antibody titers to Rauscher murine leukemia virus and mammary tumour virus
in this system; e) the retaining of activity to highly purified viral
polypeptides; f) blocking of the reaction by preincubation with rabbit
anti-mouse immunoglobulin serum or Protein A from Staphylococcus aureus.
Since germfree mice of various strains also have such antibodies, it is
concluded that the reactions are not due to horizontal transmission of the
virus. From the lack of correlation between antibody titers and tumour
incidences, it is concluded that various systems overshadow the potential
immunosurveillance role of such natural antiviral antibodies.

L17 ANSWER 2 OF 2 MEDLINE
AN 76137969 MEDLINE
DN 76137969
TI Human ***antibodies*** binding to the mouse ***mammary*** ***tumor*** ***virus*** : a nonspecific reaction?.
AU Newgard K W; Cardiff R D; Blair P B
SO CANCER RESEARCH, (1976 Feb) 36 (2 pt 2) 765-8.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197607
AB Specific rabbit antisera and over 100 human sera were found to precipitate
iodinated mouse mammary tumor virus (MTV). The specificity of these
reactions was tested in competitive inhibition studies. Three classes of
reaction could be distinguished. The Class 1 reaction was the most
specific; it could be inhibited only by MTV and was observed exclusively
with rabbit anti-MTV. The Class 2 reaction was apparently against mouse
cell determinants; it could be inhibited not only by MTV but also by mouse
lactating mammary gland and was characteristic of rabbit anti-mouse
lactating mammary gland. The Class 3 reaction was the least specific; it
could be inhibited not only by MTV and mouse lactating mammary gland but
also by dog ***milk*** . All of the human sera tested exhibited Class 3
reactivities.

=> file medline embase biosis inpadoc caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.22	5.37

FILE 'MEDLINE' ENTERED AT 10:28:48 ON 10 AUG 1999

FILE 'EMBASE' ENTERED AT 10:28:48 ON 10 AUG 1999

FILE 'BIOSIS' ENTERED AT 10:28:48 ON 10 AUG 1999

FILE 'INPADOC' ENTERED AT 10:28:48 ON 10 AUG 1999

FILE 'CAPLUS' ENTERED AT 10:28:48 ON 10 AUG 1999

AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

=> s l17

'AB' IS NOT A VALID FIELD CODE
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'AB' IS NOT A VALID FIELD CODE
L18 13 L17

=> dup rem l18

PROCESSING COMPLETED FOR L18
L19 10 DUP REM L18 (3 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L19 ANSWER 1 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1990:589384 CAPLUS
DN 113:189384
TI Mouse mammary tumor virus (MMTV) infection in SWISS and RIII mice.
Correlation between resistance to exogenous infection and anti-MMTV serum
response
AU Hainaut, P.; Vaira, Dolores; Francois, Camille; Calberg-Bacq, Claire
Michelle
CS Inst. Pathol., Univ. Liege, Liege, B-4000, Belg.
SO Arch. Virol. (1990), 113(1-2), 35-52
CODEN: ARVIDF; ISSN: 0304-8608
DT Journal
LA English
AB Host-virus relationships were examd. in mice from the mouse mammary tumor
virus (MMTV)-infected strains SWISS MB+ and RIII, which harbor the same
MMTV variant, and from the derived sublines Swiss MB- and RIIIf, which
were freed of ***milk*** -borne MMTV by foster-nursing. These 2
strains are not phylogenetically related, the SWISS strain bearing the
endogenous Mtv-3 locus in its DNA. In RIII and SWISS MB+ mice, the
incidence of early mammary tumors, which was of 96% and 8%, resp., was
correlated to the level of MMTV expression in ***milk*** . In the
SWISS MB-line, a non-coordinate expression of the provirus assocd. with
the Mtv-3 locus was obsd. in the mammary glands, the salivary glands, and
the spleen. This expression was not tumorigenic and was characterized by
the presence of the p28 gag antigen and the absence of gp52 env antigen,
except, however, in mammary glands of elder mice where traces of gp52 were
found. In the mammary glands of SWISS MB+ mice, the expression of the
Mtv-3 locus was masked by large amts. of antigens resulting from exogenous
virus expression. RIIIf mice were MMTV-neg. Viral antigens coexisted
with anti-MMTV antibodies in the serum of infected and tumor-bearing mice,
but not in the form of immune complexes. An anti-MMTV serum reactivity
was also detected in SWISS MB- and RIIIf mice. However, the serum
response was higher in the 2 SWISS lines than in the 2 RIII lines. Except
in tumor-bearing mice, the anti-MMTV response was not modified by the
presence of exogenous virus and thus resulted essentially from exposure to
endogenous MMTV expression. In exptl. infection studies, RIII mice were
more susceptible to MMTV infection than SWISS mice. The correlation
between resistance to MMTV infection and serum response to endogenous MMTV
expression, suggests that the non-tumorigenic expression of an endogenous
provirus can protect at least partially, against exogenous MMTV infection.

L19 ANSWER 2 OF 10 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1988:505990 BIOSIS
DN BA86:126674
TI THE PRESENCE OF ANTIBODIES SPECIFIC FOR MMTV STRUCTURAL PROTEINS AMONG
ANTIBODIES FROM CIRCULATING IMMUNE COMPLEXES OF BREAST CANCER PATIENTS.
AU LITVINOV S V; MALIVANOVA T F; CHUEV YU V; KRYUKOVA I N
CS ALL-UNION ONCOL. SCI. CENT., ACAD. MED. SCI. USSR, MOSCOW, USSR.
SO BYULL EKSP BIOL MED, (1988) 105 (4), 475-477.
CODEN: BEBMAE. ISSN: 0365-9615.
FS BA; OLD
LA Russian
AB Circulating immune complexes were precipitated from breast cancer
patients' sera using 2.5% polyethylenglycol. CIC isolated from 70 ml of
sera from 15 patients were dissociated and immunoglobulin-containing
fraction was prepared by chromatography on Sephadex G-200 column. The
fraction contained IgG specific for MuMTV structural proteins, as revelaed
by ELISA. CIC preparations from 22 sera of breast cancer patients were
digested with pepsin; Fab' fragment preparations were also analysed by
ELISA, only one of them was MMTV-specific. IgG and Fab' fragments isolated
from CIC reacted specifically with MMTV proteins, the reaction was not
blocked by virus-free murine ***milk*** or other retroviruses (Ra-MuLV
and MPMV).

L19 ANSWER 3 OF 10 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1985:278669 BIOSIS
DN BA79:58665
TI AUTOCHTHONOUS HUMORAL IMMUNE RESPONSES TO EXOGENOUS AND ENDOGENOUS MURINE
MAMMARY TUMOR VIRUSES IN C-3H JAX AND ICRC MICE.
AU CHIPLUNKAR S V; GANGAL S G; KARANDE K A
CS IMMUNOL. DIV., CANCER RES. INST., TATA MEML. CENT., BOMBAY 400 012, INDIA.
SO INDIAN J EXP BIOL, (1984 (RECD 1985)) 22 (12), 662-665.
CODEN: IJEBA6. ISSN: 0019-5189.
FS BA; OLD
LA English
AB Autochthonous humoral ***antibody*** response directed against murine
mammary ***tumor*** ***virus*** (MuMTV) in sera of high
mammary tumor strains of mice such as C3H(Jax), ICRC and ICRC forced
breeders and their low tumor incidence sublines C3H (Mect) and ICRCf
carrying only endogenous virus, were estimated by radioimmunoprecipitation
technique using 125I-labeled C3H MuMTV. Sera were obtained from normal
mice of various age groups, parity and lactation stage, which corresponded
to the amounts of MuMTV in the ***milk*** and also from mammary tumor
bearing mice. Highest levels of MuMTV antibodies were observed in mammary
tumor bearing mice carrying both endogenous and exogenous viruses. Mice
carrying only endogenous virus had low amounts of antibodies cross
reacting with exogenous MuMTV of C3H (Jax). A sequential increase in MuMTV
antibodies was seen in normal mice, which preceded the mammary tumor
development.

L19 ANSWER 4 OF 10 MEDLINE DUPLICATE 1
AN 81061682 MEDLINE
DN 81061682
TI Ubiquity of natural ***antibodies*** to the ***mammary*** ***tumour*** ***virus*** in mice.
AU Bentvelzen P; Brinkhof J
NC NO1 CP43328 (NCI)
SO ARCHIV FUR GESCHWULSTFORSCHUNG, (1980) 50 (3) 193-203.
Journal code: 746. ISSN: 0003-911X.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198103
AB Sera of female and male mice from eleven inbred mouse strains collected at
either 4, 12, 36 or 60 weeks of age were tested for the presence of natural ***antibodies*** to the murine ***mammary*** ***tumour*** ***virus*** by means of the Sepharose bead immunofluorescence assay. Antibodies to the virus proved to be ubiquitous,
but pronounced strain differences were found in titer and onset of antibody production. These differences were related to neither release of
virus in the ***milk*** nor susceptibility to spontaneous mammary
tumour development of a given strain. Immunological specificity of the
observed reactions was concluded from a) the failure to block the reaction
by absorption with fetal calf serum, mouse ***milk*** or sheep erythrocytes, while absorption with purified virus abolished the reactivity; b) the lack of reactivity of rat sera with the mouse mammary
tumour virus in this system; c) the negative response of mouse sera with
Sepharose beads coated with ovalbumin; d) the lack of correlation between
antibody titers to Rauscher murine leukemia virus and mammary tumour virus
in this system; e) the retaining of activity to highly purified viral polypeptides; f) blocking of the reaction by preincubation with rabbit
anti-mouse immunoglobulin serum or Protein A from Staphylococcus aureus.
Since germfree mice of various strains also have such antibodies, it is
concluded that the reactions are not due to horizontal transmission of the
virus. From the lack of correlation between antibody titers and tumour
incidences, it is concluded that various systems overshadow the potential immunosurveillance role of such natural antiviral antibodies.

L19 ANSWER 5 OF 10 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 2
AN 78304798 EMBASE
DN 1978304798
TI Detection in human breast carcinomas of an antigen immunologically related
to a group-specific antigen of mouse mammary tumor virus.
AU Mesa-Tejada R.; Keydar I.; Ramanarayanan M.; et al.
CS Inst. Cancer Res., Coll. Physcns Surg., Columbia Univ., New York, N.Y.
10032, United States
SO Proceedings of the National Academy of Sciences of the United States of
America, (1978) 75/3 (1529-1533).
CODEN: PNASA6
CY United States
DT Journal
FS 016 Cancer
010 Obstetrics and Gynecology
LA English
AB An antigen immunologically related to a group-specific antigen (gp52, a
52,000-dalton glycoprotein) of the mouse mammary tumor virus has been
identified in paraffin sections of human breast cancers by means of the
indirect immunoperoxidase technique. The specificity of the reaction with
antibody against mouse ***mammary*** ***tumor*** ***virus*** was examined by absorption of the IgG with the following:
purified gp52; a number of virus preparations (mouse mammary tumor virus,
Rauscher leukemia virus, simian sarcoma virus, baboon endogenous virus,
and Mason-Pfizer monkey virus); normal plasma, leukocytes, breast tissue,
milk , actin, collagen, and hyaluronic acid, all of human origin;
sheep erythrocytes and mucin. Only mouse mammary tumor virus (from C3H or
Paris RIII strains and grown in either murine or feline cells) and
purified gp52 eliminated the immunohistochemical reaction in the human
breast tumors. Positive reactions were seen in 51 of 131 (39%) breast
carcinomas of various histologic types, a minimal estimate in view of the
limited number of sections from each tumor that could be examined.
Negative reactions were obtained in all 119 benign breast lesions (cystic
disease, fibroadenoma, papilloma, gynecomastia) and in all 18 normal breast tissues. With 1 exception, 99 carcinomas from 13 organs other than
breast and 8 cystosarcomas were all negative.

L19 ANSWER 6 OF 10 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 79069978 EMBASE
DN 1979069978
TI Naturally occurring humoral immunity to murine mammary tumor virus (MuMTV)
and MuMTV GP52 in mice with low mammary tumor incidence.
AU Arthur L.O.; Fine D.L.
CS Viral Oncol. Progr., Frederick Cancer Res. Cent., Frederick, Md. 21701,
United States
SO International Journal of Cancer, (1978) 22/6 (734-740).
CODEN: IJCNAW
CY Switzerland
DT Journal
FS 016 Cancer
026 Immunology, Serology and Transplantation
047 Virology
LA English
SL French
AB ***Antibodies*** to murine ***mammary*** ***tumor*** ***virus*** (MuMTV) were found in sera from male and female mice by
means of a radiolabelled intact MuMTV precipitation assay. These antibodies were demonstrated both in strains of mice that have a high
incidence of mammary tumors and transmit the highly oncogenic MuMTV via
the ***milk*** (C3H) and in mice that have been foster-nursed to
remove the highly oncogenic ***milk*** -borne MuMTV (C3Hf) and
subsequently have a decreased mammary tumor incidence. Antibodies to MuMTV
were readily demonstrated in C3H mice at 6 weeks of age, whereas only
marginal antibody activity was detected in C3Hf mice of less than 15 weeks
of age. Antibody levels increased with age in both strains, but in C3Hf
mice the immune response was also accelerated by pregnancy. Several feral
and BALB/c NIV mouse sera with high (125I)MMTV precipitating titers also
precipitated the major MuMTV envelope glycoprotein (gp52). Maximum
precipitation of the (125I)gp52 was >50% with a 20% endpoint binding titer
of 1:40, whereas the same sera precipitated >80% of (125I)MMTV with a
titer of >1:2560. These naturally occurring antibodies were specific for

gp52 since only MuMTV and purified MuMTV gp52 competed for binding of
radiolabelled antigens by limiting dilutions of mouse sera. MuMTV gp52 was
found in both C3H and C3Hf mice, predominantly in organs which had
secretory functions, such as submaxillary glands and mammary tissue of
females and submaxillary, coagulating, and vesicular glands and vas
deferens of males. Extracts of other tissues were negative for MuMTV gp52.
Neither gp52 nor naturally occurring antibodies for MuMTV were found in
BALB/c or C57BL/6 mice.

L19 ANSWER 7 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1979:37410 CAPLUS
DN 90:37410
TI Modulation of mouse mammary tumor virus production in the MJY-alpha cell
line
AU Yagi, Mary Jane; Blair, Phyllis B.; Lane, Mary Ann
CS Sch. Med., Univ. Alabama, Birmingham, Ala., USA
SO J. Virol. (1978), 28(2), 611-23
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB Implantation of mouse mammary tumor virus (MMTV)-producing mammary tumor
cell line MJY-alpha into isogeneic mice elicted both humoral and T-cell
response against MMTV virion antigens. The carcinosarcomas which
developed from the implanted cells showed a decrease in MMTV synthesis,
compared with cells remaining in culture, which was detectable at
.gtoreq.7 days after implantation and for 5 transplant generations.
Electron microscopic examn. of thin sections of the tumors revealed that
intracytoplasmic A particles, budding particles, and cell-free MMTV B
particles were all affected. However, immunofluorescence assays of tumor
sections demonstrated the presence of MMTV viral antigens in the cells.
Cell cultures initiated from 1st-, 3rd-, and 4th-generation tumors were
morphol. identical to the original in vitro cell line, although virus
prodn. was barely detectable. Anal. of the cultures by electron
microscopy revealed an increase in MMTV virions after 3 in vitro passages.
Polypeptide profiles obtained by Na dodecyl sulfate-polyacrylamide gel
electrophoresis of virions purified from these cultures were identical to
MMTV. Immunodiffusion demonstrated the cross-reactivity between these
virions and MMTV particles obtained from mouse ***milk*** . In vitro
treatment of MJY-alpha cell cultures with rabbit anti-MMTV antiserum
resulted in a redn. of extracellular MMTV virions, as well as alterations
in their Na dodecyl sulfate-polyacrylamide gel electrophoretic polypeptide
patterns.

L19 ANSWER 8 OF 10 MEDLINE
AN 76137969 MEDLINE
DN 76137969
TI Human ***antibodies*** binding to the mouse ***mammary***
tumor ***virus*** : a nonspecific reaction?.
AU Newgard K W; Cardiff R D; Blair P B
SO CANCER RESEARCH, (1976 Feb) 36 (2 pt 2) 765-8.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197607
AB Specific rabbit antisera and over 100 human sera were found to precipitate
iodinated mouse mammary tumor virus (MTV). The specificity of these
reactions was tested in competitive inhibition studies. Three classes of
reaction could be distinguished. The Class 1 reaction was the most
specific; it could be inhibited only by MTV and was observed exclusively
with rabbit anti-MTV. The Class 2 reaction was apparently against mouse
cell determinants; it could be inhibited not only by MTV but also by mouse
lactating mammary gland and was characteristic of rabbit anti-mouse
lactating mammary gland. The Class 3 reaction was the least specific; it
could be inhibited not only by MTV and mouse lactating mammary gland but
also by dog ***milk*** . All of the human sera tested exhibited Class 3
reactivities.

L19 ANSWER 9 OF 10 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 77020594 EMBASE
DN 1977020594
TI Human ***antibodies*** binding to the mouse ***mammary***
tumor ***virus*** : a nonspecific reaction?.
AU Newgard K.W.; Cardiff R.D.; Blair P.B.
CS Dept. Pathol., Sch. Med., Univ. California, Davis, Calif., United States
SO Cancer Research, (1976) 36/2 (II) (765-768).
CODEN: CNREA8
DT Journal
FS 016 Cancer
047 Virology
026 Immunology, Serology and Transplantation
005 General Pathology and Pathological Anatomy
009 Surgery
LA English
AB Specific rabbit antisera and over 100 human sera were found to precipitate
iodinated mouse mammary tumor virus (MTV). The specificity of these
reactions was tested in competitive inhibition studies. Three classes of
reaction could be distinguished. The Class 1 reaction was the most
specific; it could be inhibited only by MTV and was observed exclusively
with rabbit anti MTV. The Class 2 reaction was apparently against mouse
cell determinants: it could be inhibited not only by MTV but also by mouse
lactating mammary gland and was characteristic of rabbit anti mouse
lactating mammary gland. The Class 3 reaction was the least specific; it
could be inhibited not only by MTV and mouse lactating mammary gland but
also by dog ***milk*** . All of the human sera tested exhibited Class 3
reactivities.

L19 ANSWER 10 OF 10 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 74115184 EMBASE
DN 1974115184
TI [Virus induced mammary carcinoma of mice: a genuine model of mammary
cancer in man].
DAS VIRUSINDUZIERTE MAMMAKARZINOM DER MAUS - EIN ECHTES MODELL FUR DEN
BRUSTKREBS DES MENSCHEN?.
AU Zotter S.; Muller M.
CS Pathol. Inst., Med. Akad. 'Carl Gustav Carus', Dresden, Germany
SO Deutsche Gesundheitswesen, (1973) 28/41 (1936-1942).
CODEN: DEGEA3
DT Journal
FS 005 General Pathology and Pathological Anatomy
047 Virology
016 Cancer
LA German
AB For some years the possible existence of a human mammary cancer inducing
virus has been seriously discussed. This assumption is based on the
detection of characteristic virus particles resembling the mammary tumor
virus of mice, as well as of tumor virus specific enzymes and

nucleic
acids in women's ***milk*** and mammary cancer tissue. The results of
immunologic studies, e.g. the author's own observation of specific
antibodies directed against the ***mammary*** ***tumor***
virus in the serum, above all, of women suffering from mammary
cancer and from mastopathies, complete these findings. The occurrence of
antibodies in healthy women, as well as men and children might be the
expression of a wide spreading of the hypothetic human mammary cancer
virus. The occurrence of antibodies in infected people might be regarded
as analogous to the murine mammary tumor virus. As in mice a production of
mammary tumor virus is invariably associated with formation of antibodies.
Providing a confirmation and completion of these findings, also under the
aspect of comparative tumor virology, the virus induced mammary carcinoma
of mice might well be regarded as a natural animal experimental model for
human cancer.

=> s l3

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L20 11 L3

=> dup rem l20

PROCESSING COMPLETED FOR L20
L21 7 DUP REM L20 (4 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L21 ANSWER 1 OF 7 CAPLUS COPYRIGHT 1999 ACS
AN 1998:590656 CAPLUS
DN 129:229676
TI Modified antibodies with human milk fat globule specificity for breast
cancer diagnosis and therapy
IN Do Couto, Fernando J. R.; Ceriani, Roberto L.; Peterson, Jerry A.
PA Cancer Research Fund of Contra Costa, USA
SO U.S., 76 pp. Cont.-in-part of U.S. Ser. No. 977,696.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5804187	A	19980908	US 1993-129930	19930930
US 5792852	A	19980811	US 1992-977696	19921116
WO 9411509	A2	19940526	WO 1993-US11445	19931116
WO 9411509	A3	19940707		

W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR,
LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2149529	AA	19940526	CA 1993-2149529	19931116
AU 9463964	A1	19940608	AU 1994-63964	19931116
EP 674710	A1	19951004	EP 1994-903300	19931116

R: DE, ES, FR, GB, IE, IT, NL, SE

JP 09503901	T2	19970422	JP 1993-512520	19931116

PRAI US 1992-977696 19921116
US 1993-129930 19930930
US 1993-134346 19931008
WO 1993-US11445 19931116
AB An analog peptide that comprises the variable regions of the light or
heavy chains of an antibody of a first species selectively binding to a
carcinoma antigen has 1 to 46 amino acids of the framework regions per
chain substituted with amino acids such as those present in equiv.
positions in antibodies of a species other than the first species, or
fragments thereof comprising 1 to 3 variable region CDRs per chain and
optionally flanking regions thereof of 1 to 10 or more amino acids, alone
or with an N-terminal fragment of 1 to 10 or more amino acids,
combinations or mixts. thereof. The polypeptide may also comprise an
effector agent and/or be glycosylated, and is presented as a compn. with a
carrier. The analog peptides are used in diagnostic kits for carcinomas
and methods for in vivo imaging and treating a primary or metastasized
carcinoma, and in vitro diagnosing a carcinoma, ex vivo purging neoplastic
cells from a biol. fluid. RNAs and DNAs encode the analog peptide, and a
hybrid vector carrying the nucleotides and transfected cells express the
peptides and a method produces the analog peptide. An anti-idiotype
polypeptide comprises polyclonal antibodies raised against an
anti-carcinoma antibody or the analog peptide of this invention,
monoclonal antibodies thereof, Fab, Fab', (Fab')2, CDR, variable region,
or analogs or fragments thereof, combinations thereof with an oligopeptide
comprising a TRP trimer, tandem repeats thereof, or combination or mixts.
thereof. An anti-idiotype hybrid polypeptide with an effector agent and
the anti-idiotype polypeptide, an anti-carcinoma vaccine, an
anti-carcinoma vaccination kit, a method of vaccinating against carcinoma
and a method of lowering the serum concn. of a circulating antibody or
polypeptide are provided.

L21 ANSWER 2 OF 7 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:237460 BIOSIS
DN PREV199598251760
TI Role of human ***milk*** ***antibodies*** against specific
invasion ***plasmid*** antigens (Ipas) of Shigella flexneri in
protection against invasion of HeLa cells.
AU Gomez, Henry F. (1); Forbes, Cheryl; Medellin, Christopher D.; Pickering,
Larry K.; Cleary, Thomas G.
CS (1) Dep. Peds, Univ. Texas Med. Sch., Houston, TX USA
SO Pediatric Research, (1994) Vol. 37, No. 4 PART 2, pp. 175A.
Meeting Info.: 105th Annual Meeting of the American Pediatric Society and
the 64th Annual Meeting of the Society for Pediatric Research San Diego,
California, USA May 7-11, 1995
ISSN: 0031-3998.
DT Conference
LA English

L21 ANSWER 3 OF 7 CAPLUS COPYRIGHT 1999 ACS
AN 1993:407220 CAPLUS
DN 119:7220
TI Humanized antibodies to human milk fat globules
IN Adair, John Robert; Hamann, Philip R.; Owens, Raymond John; Baker, Terence
Seward; Lyons, Alan Howard; Hinman, Lois M.; Menendez, Ana T.
PA Celltech Ltd., UK
SO Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 534742	A1	19930331	EP 1992-308680	19920924
EP 534742	B1	19971119		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
CA 2095926 AA 19930327 CA 1992-2095926 19920924
WO 9306231 A1 19930401 WO 1992-GB1759 19920924
W: AU, CA, CS, FI, HU, JP, KR, NO
AU 9225983 A1 19930427 AU 1992-25983 19920924
AU 666868 B2 19960229
EP 781845 A2 19970702 EP 1997-200482 19920924
EP 781845 A3 19970709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
AT 160362 E 19971215 AT 1992-308680 19920924
ES 2108732 T3 19980101 ES 1992-308680 19920924
IL 103269 A1 19980104 IL 1992-103269 19920924
PRAI GB 1991-20467 19910926
EP 1992-308680 19920924
WO 1992-GB1759 19920924
AB Chimeric and complementarity-detg. region (CDR)-grafted humanized antibodies to human milk fat globules are prepd. for use in the diagnosis and treatment of breast cancer. The CDRs are derived from the mouse IgG1.kappa. monoclonal antibody CTMO1 that recognizes an antigen found in high levels in blood of breast cancer patients. The antibody may be conjugated with antitumor agents for treatment of the disease. The genes for the humanized antibodies were constructed by std. methods and expressed in CHO-L761 cells. Binding and internalization of the humanized antibodies by breast carcinoma cell lines was demonstrated. Conjugation of the antibodies with calicheamicin .gamma.1I was demonstrated.

L21 ANSWER 4 OF 7 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 94031560 EMBASE
DN 1994031560
TI ***Antibodies*** to Shigella lipopolysaccharides and invasion ***plasmid*** antigens in colostrum and breast ***milk*** of women from Puriscal, a rural area of Costa Rica.
AU Achi R.A.; Vives M.; Garcia M.E.; Binh Minh N.; Mata L.; Lindberg A.A.
CS Department of Clinical Bacteriology, Huddinge Hospital, Karolinska Institute,S-141 81 Huddinge, Sweden
SO Serodiagnosis and Immunotherapy in Infectious Disease, (1993) 5/4 (237-244).
ISSN: 0888-0786 CODEN: SIIDE3
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
LA English
SL English
AB Specific antibody titres of colostrum and breast milk from 208 healthy women of Puriscal, a rural area of Costa Rica, were determined by enzyme immunoassays. Mean relative IgA titres of 790 .+-. SD = 640 (ranges = 70-3250), 440 .+-. 490 (40-2940), and 280 .+-. 230 (10-1000) to Shigella flexneri, Shigella sonnei and Shigella dysenteriae type 1 lipopolysaccharides (LPSs), respectively, were found in colostrum on day 1 post delivery. Titres declined thereafter and only relatively low values were found on days 30, 90 and 180 post partum. Mean IgA anti-invasion plasmid antigens (Ipa) titres of 200 .+-. 230, 140 .+-. 170 and 120 .+-. 190 on days 1-2, 3-4 and 5-8 post delivery were found, respectively. Thereafter the anti-Ipa titres were low. IgM antibody titres were found against the LPS antigens but not to the Ipa. IgG antibody titres were low against both LPS and Ipa, with the exception of four out of 59 (7%) at day 1, with titres to the S. flexneri Y LPS and three out of 59 (5%) at day 1 and one out of 87 (1%) at days 3-4, with positive IgG titres to Ipa. By using a cut off value (mean +2 sD established for a high socioeconomic status group of Costa Rica), 20%, 17% and 5% of colostrum samples, at day 1, had high titres to S. flexneri, S. sonnei and S. dysenteriae, respectively. A good degree of correlation between colostrum IgA anti-S. flexneri Y LPS and the anti-Ipa antibodies, was found. The colostrum antibody titres (day 1) of mothers from Puriscal were intermediate as compared to mothers from the low and the high socioeconomic conditions in the metropolitan area of Costa Rica and tended to be lower than in Vietnamese mothers from endemic areas of shigellosis. Shigella exposure seems to be lower in this rural region than in overcrowded slums of San Jose, Costa Rica.

L21 ANSWER 5 OF 7 MEDLINE DUPLICATE 1
AN 93078105 MEDLINE
DN 93078105
TI Concentration of ***milk*** secretory ***immunoglobulin*** A against Shigella virulence ***plasmid*** -associated antigens as a predictor of symptom status in Shigella-infected breast-fed infants.
AU Hayani K C; Guerrero M L; Morrow A L; Gomez H F; Winsor D K; Ruiz-Palacios G M; Cleary T G
CS Department of Pediatrics, University of Texas Medical School, Houston 77030.
NC 5-PO1-HD-13021 (NICHD)
SO JOURNAL OF PEDIATRICS, (1992 Dec) 121 (6) 852-6.
Journal code: JLZ. ISSN: 0022-3476.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199303
AB We conducted a prospective, community-based study of healthy breast-fed Mexican infants to determine the protective effects of anti-Shigella secretory IgA antibodies in milk. Milk samples were collected monthly, and stool culture specimens were obtained weekly and at the time of episodes of diarrhea. Nineteen breast-fed infants were found to have Shigella flexneri, Shigella boydii, or Shigella sonnei in stool samples. Ages of the 10 infants with symptomatic infection and the nine with asymptomatic infection did not differ significantly. Milk samples collected up to 12 weeks before infection were evaluated by enzyme-linked immunosorbent assay for secretory IgA antibodies against lipopolysaccharides of S. flexneri, S. boydii serotype 2, S. sonnei, and virulence plasmid-associated antigens. The geometric mean titers of anti-Shigella ***antibodies*** to virulence ***plasmid*** -associated antigens in ***milk*** received before infection were eightfold higher in infants who remained well than in those in whom diarrhea developed. The significance of milk secretory IgA directed against lipopolysaccharide was less clear. We conclude that human milk protects infants against symptomatic shigella infection when it contains high concentrations of secretory IgA against virulence plasmid-associated antigens.

L21 ANSWER 6 OF 7 CAPLUS COPYRIGHT 1999 ACS
AN 1993:145584 CAPLUS
DN 118:145584
TI Milk secretory IgA related to Shigella virulence antigens
AU Cleary, Thomas G.; Hyani, Karen; Winsor, Donald K.;

Ruiz-Palacios,
Guillermo
CS Med. Sch., Univ. Texas, Houston, TX, USA
SO Adv. Exp. Med. Biol. (1991), 310(Immunol. Milk Neonate), 369-73
CODEN: AEMBAP; ISSN: 0065-2598
DT Journal
LA English
AB Human milk commonly contains antibodies to the major virulence antigens
shared by all Shigellae. The levels of these antibodies in milk do not
change significantly during lactation either in a high (Mexico) or low
Shigella risk population (US). The presence of ***antibodies*** to
Shigella virulence ***plasmid*** -coded antigens in the ***milk***
of women from an area where Shigella infection is not common suggests that
Shigella-specific, IgA-secreting cells which have been programmed in the
distant past are recruited to the breast during pregnancy or lactation.

L21 ANSWER 7 OF 7 MEDLINE DUPLICATE 2
AN 91093893 MEDLINE
DN 91093893
TI Human ***milk*** secretory ***immunoglobulin*** A to Shigella
virulence ***plasmid*** -coded antigens.
AU Cleary T G; West M S; Ruiz-Palacios G; Winsor D K; Calva J J; Guerrero M
L; Van R
CS Department of Pediatrics and Microbiology, University of Texas Medical
School at Houston 77030..
NC 5-PO1-HD-13021 (NICHD)
SO JOURNAL OF PEDIATRICS, (1991 Jan) 118 (1) 34-8.
Journal code: JLZ. ISSN: 0022-3476.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199104
AB Although antibodies to the lipopolysaccharide antigens of Shigella have
been demonstrated in human milk, such antibodies do not explain the
putative protective effect of breast-feeding against symptomatic Shigella
infection. Shigella species do not share related lipopolysaccharides, but
they do possess closely related virulence plasmids that code for the
proteins essential for cell invasion. We therefore sought to determine the
frequency, amount, and duration of excretion of human ***milk***
antibodies to these shared virulence ***plasmid*** -associated
antigens in populations of different rates of Shigella infection frequency
(Mexico City, high; Houston, low). Such antibodies were present in the
milk of virtually all the Mexican women but also were present in a large
proportion of milk samples from the women living in Houston. The amounts
of these antibodies were highest in colostrum but after 2 weeks of
lactation fell to stable levels. The frequency and persistence of these
antibodies in the milk of the women from Houston suggest that the memory
and drive for secretion of these antibodies is extremely long lived.

=> s l5

'AB' IS NOT A VALID FIELD CODE
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'AB' IS NOT A VALID FIELD CODE
L22 5 L5

=> dup rem l22

PROCESSING COMPLETED FOR L22
L23 5 DUP REM L22 (0 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L23 ANSWER 1 OF 5 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:242446 BIOSIS
DN PREV199598256746
TI ***Recombinant*** ***immunoglobulin*** A expressed in a mouse
mammary gland cell line.
AU Rindisbacher, L. (1); Berdoz, J.; Jeanguenat, N.; Corthesy, B. (1);
Kraehenbuehl, J.-P.
CS (1) Inst. Biol. Animale, Univ. Lausanne, Lausanne Switzerland
SO Experientia (Basel), (1995) Vol. 51, No. ABSTR., pp. A77.
Meeting Info.: 27th Annual Meeting of the Swiss Societies for Experimental
Biology (USGEB/USSBE) Fribourg, Switzerland March 30-31, 1995
ISSN: 0014-4754.
DT Conference
LA English

L23 ANSWER 2 OF 5 CAPLUS COPYRIGHT 1999 ACS
AN 1991:88772 CAPLUS
DN 114:88772
TI Recombinant ricin A chain-monoclonal antibody conjugates for cancer
targeting therapy
IN Frankel, Arthur E.
PA Cetus Corp., USA
SO U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 806,256, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4962188	A	19901009	US 1986-913357	19860930
CA 1287578	A1	19910813	CA 1986-524645	19861205
JP 62209098	A2	19870914	JP 1986-289791	19861206
US 4956453	A	19900911	US 1987-69720	19870706

PRAI US 1985-806256 19851206
AB The title conjugates comprising unglycosylated recombinant ricin A chain
and monoclonal antibodies (MAbs) to e.g. ovarian cancer are manufd. and
characterized. The conjugates are maintained at an effective cytotoxic
amt. in the circulation of a host animal for substantially longer times
than similar conjugates contg. native ricin A chain from, e.g., caster
beans. The conjugates of the invention are cleared .apprx.9 times slower
from the circulation of a host animal than conjugates prepd. from native
ricin A chain. Prodn. of the MAbs also is described.

L23 ANSWER 3 OF 5 CAPLUS COPYRIGHT 1999 ACS
AN 1991:40618 CAPLUS
DN 114:40618
TI Vaccination against tumor cells expressing breast cancer epithelial tumor
antigen
AU Hareuveni, Mara; Gautier, Claudie; Kieny, Marie Paule; Wreschner, Daniel;
Chambon, Pierre; Lathe, Richard
CS Lab. Genet. Mol. Eucaryotes, Inst. Chim. Biol., Strasbourg, 67085, Fr.
SO Proc. Natl. Acad. Sci. U. S. A. (1990), 87(23), 9498-502
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Ninety-one percent of breast tumors aberrantly express an epithelial tumor
antigen (ETA) identified by monoclonal antibody H23. Vaccinia virus
recombinants expressing tumor antigens have considerable promise in the
active immunotherapy of cancer, and the authors have evaluated the

potential of vaccinia recombinants expressing the secreted (S) and cell-assocd. (transmembrane, T) forms of H23 ETA to elicit immunity to tumor cells expressing ETA. Tumorigenic ras-transformed Fischer rat fibroblast lines FR-S and FR-T, expressing the S or T form of H23 ETA, resp., were constructed for use in challenge expts. Expression of H23 ETA in these lines was confirmed by Western blotting and immunofluorescence. When challenged by s.c. seeding of tumor cells, 97% (FR-S) and 91% (FR-T) of syngeneic Fischer rats rapidly developed tumors that failed to regress. Vaccination with recombinant vaccinia virus expressing ETA-T prior to challenge prevented tumor development in 82% of animals seeded with FR-T cells but in only 61% of animals seeded with FR-S. The vaccinia recombinant expressing the S form was a less effective immunogen, and vaccination protected only 29-30% of animals from developing tumors upon challenge with either FR-S or -T cells. The increased immunogenicity of the recombinant expressing ETA-T was reflected in elevated levels of ETA-reactive antibody in vaccinated animals, confirming that secreted antigens expressed from vaccinia virus are less effective immunogens than their membrane-assocd. counterparts.

L23 ANSWER 4 OF 5 CAPLUS COPYRIGHT 1999 ACS
AN 1989:188523 CAPLUS
DN 110:188523
TI Characterization and biodistribution of recombinant and recombinant/chimeric constructs of monoclonal antibody B72.3
AU Colcher, David; Milenic, Diane; Roselli, Mario; Raubitschek, Andrew; Yarranton, Geoffrey; King, David; Adair, John; Whittle, Nigel; Bodmer, Mark; Schlom, Jeffrey
CS Radiat. Oncol. Branch, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Cancer Res. (1989), 49(7), 1738-45
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
AB B72.3 is a murine monoclonal antibody (IgG1) that recognizes a tumor-assocd. glycoprotein, termed TAG-72. B72.3 has been shown, using a variety of methodologies, to have a high degree of selective reactivity for colorectal, ovarian, lung, and breast carcinomas. Radiolabeled B72.3 has been administered both i.v. and i.p. in patients with colorectal and ovarian cancer as well as other carcinomas and has been shown to selectively bind to .apprx.70-80% of metastatic lesions. Greater than 50% of the patients that have been treated with B72.3 have developed an immunol. response to murine IgG after a single injection. In an attempt to minimize the immune response of these patients to the administered murine monoclonal antibody, a recombinant form of the murine B72.3 has been developed as well as a recombinant/chimeric antibody, using the variable regions of the murine B72.3 and human heavy chain (.gamma.4) and light chain (.kappa.) const. regions. It is reported here that both the recombinant B72.3 [rB72.3] and the recombinant/chimeric B72.3 [cB72.3(.gamma.4)] iGGs maintain the tissue binding and idiotypic specificity of the native murine IgG. The native B72.3, rB72.3, and cB72.3(.gamma.4) IgGs were radiolabled and the biodistribution of these IgGs was studied in athymic mice bearing human colon carcinoma xenografts (LS-174T). Differences were obsd. between the cB72.3(.gamma.4) and the native B72.3 in the percent of injected dose/g that localized in the tumor. The somewhat lower abs. amts. of the cB72.3(.gamma.4) in the tumor are most likely due to the obsd. more rapid clearance from the blood and body of the mouse as compared to the native B72.3 and rB72.3. All 3 forms [native B72.3, rB72.3, and cB72.3(.gamma.4)] of the IgG, however, able to localize the colon tumor with similar radiolocalization indexes [percent of injected dose/g in tumor divided by the percent of injected dose/g in normal tissue].

L23 ANSWER 5 OF 5 CAPLUS COPYRIGHT 1999 ACS
AN 1988:400354 CAPLUS
DN 109:354
TI Response of primary human mammary tumor cell cultures to a monoclonal antibody-recombinant ricin A chain immunotoxin
AU Bjorn, Michael J.; Smith, Helene S.; Dairkee, Shahnaz H.
CS Dep. Protein Chem., Cetus Corp., Emeryville, CA, 94608, USA
SO Cancer Immunol. Immunother. (1988), 26(2), 121-4
CODEN: CIIMDN; ISSN: 0340-7004
DT Journal
LA English
AB Malignant epithelial tumor cells were isolated and cultured from 10 human mammary specimens of cancerous origin. The 260F9 monoclonal antibody (MAB) bound to frozen sections of all 10 tumors tested and to primary cultured cells from the tumors. Cultured cells from all 10 tumors were sensitive to the clonal inhibitory effects of immunotoxin 260F9 MAB-recombinant ricin A chain. At the immunotoxin concn. of 200 ng/mL (about 1 nM), the inhibition of colony formation was >99% for all 10 tumors.

=> d 2 kwic

L23 ANSWER 2 OF 5 CAPLUS COPYRIGHT 1999 ACS
IT ***Mammary*** gland
(neoplasm, monoclonal ***antibody*** to, ***recombinant***
ricin A chain conjugate with, for targeting therapy)

=> s l7

'AB' IS NOT A VALID FIELD CODE
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'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L24 4 L7

=> dup rem l24

PROCESSING COMPLETED FOR L24
L25 4 DUP REM L24 (0 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L25 ANSWER 1 OF 4 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:242446 BIOSIS
DN PREV199598256746
TI ***Recombinant*** ***immunoglobulin*** A expressed in a mouse ***mammary*** gland cell line.
AU Rindisbacher, L. (1); Berdoz, J.; Jeanguenat, N.; Corthesy, B. (1); Kraehenbuehl, J.-P.
CS (1) Inst. Biol. Animale, Univ. Lausanne, Lausanne Switzerland
SO Experientia (Basel), (1995) Vol. 51, No. ABSTR., pp. A77.
Meeting Info.: 27th Annual Meeting of the Swiss Societies for Experimental Biology (USGEB/USSBE) Fribourg, Switzerland March 30-31, 1995
ISSN: 0014-4754.
DT Conference
LA English

L25 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS
AN 1991:88772 CAPLUS
DN 114:88772
TI Recombinant ricin A chain-monoclonal antibody conjugates for cancer
targeting therapy
IN Frankel, Arthur E.
PA Cetus Corp., USA
SO U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 806,256, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4962188	A	19901009	US 1986-913357	19860930
CA 1287578	A1	19910813	CA 1986-524645	19861205
JP 62209098	A2	19870914	JP 1986-289791	19861206
US 4956453	A	19900911	US 1987-69720	19870706
PRAI US 1985-806256		19851206		

AB The title conjugates comprising unglycosylated recombinant ricin A chain
and monoclonal antibodies (MAbs) to e.g. ovarian cancer are manufd. and
characterized. The conjugates are maintained at an effective cytotoxic
amt. in the circulation of a host animal for substantially longer times
than similar conjugates contg. native ricin A chain from, e.g., caster
beans. The conjugates of the invention are cleared .apprx.9 times slower
from the circulation of a host animal than conjugates prepd. from native
ricin A chain. Prodn. of the MAbs also is described.

L25 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS
AN 1989:188523 CAPLUS
DN 110:188523
TI Characterization and biodistribution of recombinant and
recombinant/chimeric constructs of monoclonal antibody B72.3
AU Colcher, David; Milenic, Diane; Roselli, Mario; Raubitschek, Andrew;
Yarranton, Geoffrey; King, David; Adair, John; Whittle, Nigel; Bodmer,
Mark; Schlom, Jeffrey
CS Radiat. Oncol. Branch, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Cancer Res. (1989), 49(7), 1738-45
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
AB B72.3 is a murine monoclonal antibody (IgG1) that recognizes a
tumor-assocd. glycoprotein, termed TAG-72. B72.3 has been shown, using a
variety of methodologies, to have a high degree of selective reactivity
for colorectal, ovarian, lung, and breast carcinomas. Radiolabeled B72.3
has been administered both i.v. and i.p. in patients with colorectal and
ovarian cancer as well as other carcinomas and has been shown to
selectively bind to .apprx.70-80% of metastatic lesions. Greater than 50%
of the patients that have been treated with B72.3 have developed an
immunol. response to murine IgG after a single injection. In an attempt
to minimize the immune response of these patients to the administered
murine monoclonal antibody, a recombinant form of the murine B72.3 has
been developed as well as a recombinant/chimeric antibody, using the
variable regions of the murine B72.3 and human heavy chain (.gamma.4) and
light chain (.kappa.) const. regions. It is reported here that both the
recombinant B72.3 [rB72.3] and the recombinant/chimeric B72.3
[cB72.3(.gamma.4)] iGGs maintain the tissue binding and idiotypic
specificity of the native murine IgG. The native B72.3, rB72.3, and
cB72.3(.gamma.4) IgGs were radiolabled and the biodistribution of these
IgGs was studied in athymic mice bearing human colon carcinoma xenografts
(LS-174T). Differences were obsd. between the cB72.3(.gamma.4) and the
native B72.3 in the percent of injected dose/g that localized in the
tumor. The somewhat lower abs. amts. of the cB72.3(.gamma.4) in the tumor
are most likely due to the obsd. more rapid clearance from the blood and
body of the mouse as compared to the native B72.3 and rB72.3. All 3 forms
[native B72.3, rB72.3, and cB72.3(.gamma.4)] of the IgG, however, able to
localize the colon tumor with similar radiolocalization indexes [percent
of injected dose/g in tumor divided by the percent of injected dose/g in
normal tissue].

L25 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS
AN 1988:400354 CAPLUS
DN 109:354
TI Response of primary human mammary tumor cell cultures to a monoclonal
antibody-recombinant ricin A chain immunotoxin
AU Bjorn, Michael J.; Smith, Helene S.; Dairkee, Shahnaz H.
CS Dep. Protein Chem., Cetus Corp., Emeryville, CA, 94608, USA
SO Cancer Immunol. Immunother. (1988), 26(2), 121-4
CODEN: CIIMDN; ISSN: 0340-7004
DT Journal
LA English
AB Malignant epithelial tumor cells were isolated and cultured from 10 human
mammary specimens of cancerous origin. The 260F9 monoclonal antibody
(MAB) bound to frozen sections of all 10 tumors tested and to primary
cultured cells from the tumors. Cultured cells from all 10 tumors were
sensitive to the clonal inhibitory effects of immunotoxin 260F9
MAB-recombinant ricin A chain. At the immunotoxin concn. of 200 ng/mL
(about 1 nM), the inhibition of colony formation was >99% for all 10
tumors.

=> d 3 kwic

L25 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS
IT ***Mammary*** gland
(neoplasm, carcinoma, radioiodinated monoclonal ***antibody***
recombinant and ***recombinant*** /chimeric constructs
metab. by, scintigraphy in relation to)

=> s l9

'AB' IS NOT A VALID FIELD CODE
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'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L26 0 L9

=> s l11

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L27 1 L11

=> d bib ab

L27 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
AN 1989:188523 CAPLUS
DN 110:188523
TI Characterization and biodistribution of recombinant and
recombinant/chimeric constructs of monoclonal antibody B72.3
AU Colcher, David; Milenic, Diane; Roselli, Mario; Raubitschek, Andrew;
Yarranton, Geoffrey; King, David; Adair, John; Whittle, Nigel; Bodmer,
Mark; Schlom, Jeffrey
CS Radiat. Oncol. Branch, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Cancer Res. (1989), 49(7), 1738-45

CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
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=> d kwic

L27 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
IT ***Mammary*** gland
(neoplasm, carcinoma, radioiodinated monoclonal ***antibody***
recombinant and ***recombinant*** /chimeric ***constructs*** metab. by, scintigraphy in relation to)

=> s l11

'AB' IS NOT A VALID FIELD CODE
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'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L28 1 L11

=> d

L28 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
AN 1989:188523 CAPLUS
DN 110:188523
TI Characterization and biodistribution of recombinant and recombinant/chimeric constructs of monoclonal antibody B72.3
AU Colcher, David; Milenic, Diane; Roselli, Mario; Raubitschek, Andrew; Yarranton, Geoffrey; King, David; Adair, John; Whittle, Nigel; Bodmer, Mark; Schlom, Jeffrey
CS Radiat. Oncol. Branch, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Cancer Res. (1989), 49(7), 1738-45
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English

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'AB' IS NOT A VALID FIELD CODE
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3 FILES SEARCHED...
'AB' IS NOT A VALID FIELD CODE
L29 9 L12

=> dup rem l29

PROCESSING COMPLETED FOR L29
L30 4 DUP REM L29 (5 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L30 ANSWER 1 OF 4 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:409805 BIOSIS
DN PREV199800409805
TI Cloning, expression, and characterization of recombinant Fab antibodies against dioxin.
AU Lee, Nanju (1); Holtzapple, Carol K.; Stanker, Larry H.
CS (1) Food Anim. Protection Res. Lab., Agricultural Res. Service, U.S. Dep. Agriculture, 2881 F and B Road, College Station, TX 77845-9594 USA
SO Journal of Agricultural and Food Chemistry, (Aug., 1998) Vol. 46, No. 8, pp. 3381-3388.
ISSN: 0021-8561.
DT Article
LA English
AB Using two hybridoma cell lines (DD1 and DD3) secreting anti-dioxin monoclonal antibodies as a source for messenger RNA and cDNA, light and heavy chain gene fragments of Fab domains were amplified by the polymerase chain reaction (PCR). The amplified gene fragments were cloned into the pFabUSDAI ***vector*** for expression of ***recombinant*** Fab ***antibodies*** in Escherichia coli. Expression of the soluble and ***functional*** recombinant Fab antibodies (designated rFab1-1 and rFab3-3) was confirmed by an indirect immunoassay using dioxin conjugated to rabbit serum albumin. On the basis of these rFabs, two competitive inhibition immunoassays using 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) as a competitor were developed. The concentration of 2,3,7,8-TCDD required to inhibit color development by 50% (IC50) determined from the dose response curves for rFAB1-1 and rFAB3-3 were 10.4 +- 2.4 and 12.2 +- 6.0 ng/mL, respectively. The binding properties of both rFab antibodies for other chemically related compounds were relatively similar to those of their respective monoclonal antibodies and enzymatically derived Fab fragments.

L30 ANSWER 2 OF 4 MEDLINE DUPLICATE 1
AN 1998455662 MEDLINE
DN 98455662
TI Isolation and recombinant expression of an MHV-JHM neutralising monoclonal antibody.
AU Kolb A F; Lechermaier M; Heister A; Toksoy A; Siddell S G
CS Institute of Virology and Immunology, University of Wurzburg, Germany.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 440 657-64.
Journal code: 2LU. ISSN: 0065-2598.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
EW 19990303
AB The monoclonal antibody A1 (mab A1) efficiently neutralises the infection
of susceptible cells by the murine hepatitis virus MHV-JHM in vitro and in
vivo (Wege et al., 1984). The variable regions of mab A1 were amplified
from mRNA of the respective hybridoma cell line by RT-PCR and integrated
into different eukaryotic expression vectors. The biological
function of the ***recombinant*** ***antibody***
constructs was verified by virus neutralisation assays. Whereas a
complete recombinant antibody (mab A1rec.) expressed in transfected murine
myeloma cells inhibited the MHV-JHM infection as well as the parental
antibody, a single-chain Fv derived from mab A1 did not show any
neutralising activity.

L30 ANSWER 3 OF 4 MEDLINE DUPLICATE 2
AN 97041563 MEDLINE
DN 97041563
TI Lung cancer-reacting human recombinant antibody AE6F4: potential
usefulness in the sputum cytodiagnosis.
AU Shoji M; Kawamoto S; Seki K; Teruya K; Setoguchi Y; Mochizuki K; Kato M;
Hashizume S; Hanagiri T; Yoshimatsu T; Nakanishi K; Yasumoto K; Nagashima
A; Nakahashi H; Suzuki T; Imai T; Shirahata S; Nomoto K; Murakami H
CS Morinaga Institute of Biological Science, Yokohama, Japan.
SO HUMAN ANTIBODIES AND HYBRIDOMAS, (1996) 7 (1) 27-36.
Journal code: A6A. ISSN: 0956-960X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
EW 19970601
AB Human monoclonal antibody (hMAb) AE6F4 has been shown to be potentially
useful for immunocytological detection of lung cancer cells in sputum. By
recombinant DNA technology, IgM type hMAb AE6F4 was switched to IgG. The
IgG mimic ***recombinant*** AE6F4 ***antibody*** expression
plasmid was ***assembled*** using the ***antibody*** heavy
chain gene, which ligated the gene encoding VH and CH1(mu) domains of hMAb
AE6F4 heavy chain to the gene encoding CH2(gamma 1) and CH3(gamma 1)
domains of human IgG heavy chain, and the antibody light chain gene of
hMAb AE6F4. The recombinant antibody expressed by baby hamster kidney
(BHK)-21 cells showed molecular size equivalence to IgG, and consisted of
human mu-gamma hybrid heavy and kappa light chains. The immunological
specificity of the recombinant antibody was the same as that of hMAb AE6F4
by immunoblotting analysis to the 14-3-3 protein, the putative antigen of
hMAb AE6F4, and by immunohistochemical and immunocytological analyses
using tissue sections and sputa of lung cancer patients. The transfected
BHK-21 cells produced the recombinant antibody persistently and the
productivity was greater than 20 times that by human-human hybridoma
producing hMAb AE6F4.

L30 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS
AN 1992:631697 CAPLUS
DN 117:231697
TI Cloning, bacterial expression and crystallization of Fv antibody fragments
AU Eisele, Jean Luc; Boulot, Ginette; Chitarra, Veronique; Riottot, Marie
Madeleine; Souchon, Helene; Houdusse, Anne; Bentley, Graham A.; Bhat, T.
Narayana; Spinelli, Silvia; Poljak, Roberto J.
CS Dep. Immunol., Inst. Pasteur, Paris, F-75724, Fr.
SO J. Cryst. Growth (1992), 122(1-4), 337-43
CODEN: JCRGAE; ISSN: 0022-0248
DT Journal; General Review
LA English
AB A review, with 16 refs., of the author's work on the variable Fv fragments
of ***antibodies*** , cloned in ***recombinant*** ***plasmids***
, and expressed in bacteria as ***functional*** proteins having immunochem. properties similar or identical with those of the corresponding parts of the parent eukaryotic antibodies.

=> s l13

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L31 0 L13

=> s l15

'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L32 0 L15

=> d his

(FILE 'HOME' ENTERED AT 10:20:31 ON 10 AUG 1999)

FILE 'MEDLINE' ENTERED AT 10:20:36 ON 10 AUG 1999
L1 583923 S IMMUNOGLOB? OR ANTIBOD?/AB,BI
L2 843 S L1(5A)(CONSTRUCT# OR PLASMID# OR VECTOR#)/AB,BI
L3 2 S L2(5A)(MILK)/AB,BI
L4 357 S L1(5A)(MAMMARY)
L5 0 S L4(10A)(RECOMBINANT)
L6 357 S L1(5A)(MAMMARY)/AB,BI
L7 0 S L6(5A)(RECOMBINANT)/AB,BI
L8 33 S L6(5A)(SPECIFIC)/AB,BI
L9 0 S L8 AND PROMOTER#/AB,BI
L10 57 S L2(5A)(RECOMBIN?)/AB,BI
L11 0 S L10(5A)(MILK OR MAMMARY)/AB,BI
L12 2 S L10(10A)(FUNCTION? OR ASSEMBL?)/AB,BI
L13 0 S L2(5A)(MAMMARY)(W)(TUMOR OR TUMOUR)/AB,BI
L14 74 S L1(5A)(MAMMARY)(W)(TUMOR OR TUMOUR)/AB,BI
L15 0 S L14(5A)(PROMOTER#)/AB,BI
L16 42 S L14(5A)(VIRUS)/AB,BI
L17 2 S L16 AND MILK/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 10:28:48 ON 10
AUG 1999
L18 13 S L17
L19 10 DUP REM L18 (3 DUPLICATES REMOVED)
L20 11 S L3
L21 7 DUP REM L20 (4 DUPLICATES REMOVED)
L22 5 S L5
L23 5 DUP REM L22 (0 DUPLICATES REMOVED)
L24 4 S L7
L25 4 DUP REM L24 (0 DUPLICATES REMOVED)
L26 0 S L9
L27 1 S L11
L28 1 S L11
L29 9 S L12
L30 4 DUP REM L29 (5 DUPLICATES REMOVED)
L31 0 S L13
L32 0 S L15

=>

---Logging off of STN---

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 ********************************
FILE 'USPAT' ENTERED AT 09:28:32 ON 10 AUG 1999

 ********************************
 *     U.S. PATENT TEXT FILE      *
 *                                *
 * THE WEEKLY PATENT TEXT AND IMAGE DATA IS
CURRENT        *
 * THROUGH AUGUST 10,1999                 *
 *                                *
 *                                *
 ********************************

=> s mammary tumor

      4414 MAMMARY
     22585 TUMOR
L1    1307 MAMMARY TUMOR
        (MAMMARY(W)TUMOR)

=> s l1(5a)(promoter)

     27962 PROMOTER
L2     202 L1(5A)(PROMOTER)

=> s l2(10a)(antibod? or immunoglobulin#)

     36150 ANTIBOD?
     11405 IMMUNOGLOBULIN#
L3       1 L2(10A)(ANTIBOD? OR IMMUNOGLOBULIN#)

=> d


1. 5,733,768, Mar. 31, 1998, Amyloid precursor protein protease; Eric
P.
Dixon, et al., 435/226 [IMAGE AVAILABLE]

=> s mammary(5a)(promoter#)

      4414 MAMMARY
     36145 PROMOTER#
L4     299 MAMMARY(5A)(PROMOTER#)

=> s l4(10a)(antibod? or immunoglob? or chain#)

     36150 ANTIBOD?
     11609 IMMUNOGLOB?
    343081 CHAIN#
L5       3 L4(10A)(ANTIBOD? OR IMMUNOGLOB? OR
CHAIN#)

=> d l- cit ab


1. 5,919,650, Jul. 6, 1999, Method for inactivation of protein function;
Mariano Barbacid, et al., 435/69.1, 320.1, 330 [IMAGE
AVAILABLE]

US PAT NO:  5,919,650 [IMAGE AVAILABLE]      L5: 1 of 3

ABSTRACT:
Method for inactivating the function produced by a protein using an
intracellularly expressed antibody or fragment thereof.


2. 5,880,327, Mar. 9, 1999, Transgenic mammals expressing human
coagulation factor VIII; Henryk Lubon, et al., 800/7; 435/455; 800/4,
14,
15, 16, 17, 18, 21, 24, 25 [IMAGE AVAILABLE]

US PAT NO:  5,880,327 [IMAGE AVAILABLE]      L5: 2 of 3

ABSTRACT:
A non-human transgenic mammalian animal, as described above,
contains an
exogenous double stranded DNA sequence stably integrated into the
genome
of the animal, which comprises cis-acting regulatory units operably
linked to a DNA sequence encoding human Factor VIII protein and a
signal
peptide, where the cis-acting regulatory units are active in mammary
gland cells and the signal peptide is active in directing newly
expressed
Factor VIII into the milk of the animal. The promoter may be a milk
protein promoter such as for whey acidic protein, casein, lactalbumin,
or
beta-lactoglobulin promoter. The transgenic mammals are preferably
farm
animals, for example, cows, goats, sheep, rabbits and pigs. Concurrent
expression of a gene for human von Willebrand's Factor into milk may
be
used to stabilize newly-secreted Factor VIII.


3. 5,733,768, Mar. 31, 1998, Amyloid precursor protein protease; Eric
P.
Dixon, et al., 435/226 [IMAGE AVAILABLE]

US PAT NO:  5,733,768 [IMAGE AVAILABLE]      L5: 3 of 3

ABSTRACT:
This invention provides an APP-cleaving protein and related nucleic
acid
compounds. The invention also provides methods, materials and
assays. The
compounds of this invention will further the characterization of
neurological diseases such as Alzheimer's disease and Down's
syndrome.

=> s mouse mammary

     46615 MOUSE
      4414 MAMMARY
L6     888 MOUSE MAMMARY
        (MOUSE(W)MAMMARY)

=> s l6(5a)(promoter#)

     36145 PROMOTER#
L7     210 L6(5A)(PROMOTER#)

=> s l7(5a)(immunoglob? or antibod? or chain#)

     11609 IMMUNOGLOB?
     36150 ANTIBOD?
    343081 CHAIN#
L8       1 L7(5A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)

=> d


1. 5,733,768, Mar. 31, 1998, Amyloid precursor protein protease; Eric
P.
Dixon, et al., 435/226 [IMAGE AVAILABLE]

=> d kwic


US PAT NO:  5,733,768 [IMAGE AVAILABLE]      L8: 1 of 1

SUMMARY:

BSUM(64)

 The . . . Promoters which my be used, for example, are the
thymidine
kinase promoter, the metallothionin promoter, the heat shock
promoter,
the **mouse** **mammary** tumor virus **promoter** or various
other vital
and **immunoglobulin** promoters.

=> s tumor virus promoter#

     22585 TUMOR
     24029 VIRUS
     36145 PROMOTER#
L9     74 TUMOR VIRUS PROMOTER#
        (TUMOR(W)VIRUS(W)PROMOTER#)

=> s l9(5a)(mammary)

      4414 MAMMARY
L10     74 L9(5A)(MAMMARY)

=> s l10(10a)(immunoglob? or antibod? or chain#)

     11609 IMMUNOGLOB?
     36150 ANTIBOD?
    343081 CHAIN#
L11      1 L10(10A)(IMMUNOGLOB? OR ANTIBOD? OR
```

CHAIN#)

=> d

1. 5,733,768, Mar. 31, 1998, Amyloid precursor protein protease; Eric P.
Dixon, et al., 435/226 [IMAGE AVAILABLE]

=> file epoab

FILE 'EPOABS' ENTERED AT 09:36:47 ON 10 AUG 1999

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 ********************************
 *  EUROPEAN PATENT ABSTRACTS   *
 ********************************
```

=> s l11

```
      2533 TUMOR
      3729 VIRUS
      3960 PROMOTER#
         0 TUMOR VIRUS PROMOTER#
           (TUMOR(W)VIRUS(W)PROMOTER#)
       254 MAMMARY
       894 IMMUNOGLOB?
      9129 ANTIBOD?
     39372 CHAIN#
L12       0 L10(10A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)
```

=> s (metalloth?)(3a)(promoter#)

```
        67 METALLOTH?
      3960 PROMOTER#
L13      13 (METALLOTH?)(3A)(PROMOTER#)
```

=> s l13(10a)(mammary)

```
       254 MAMMARY
L14       0 L13(10A)(MAMMARY)
```

=> file uspat

FILE 'USPAT' ENTERED AT 09:37:55 ON 10 AUG 1999

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 ********************************
 *     U.S. PATENT TEXT FILE    *
 *                              *
 * THE WEEKLY PATENT TEXT AND IMAGE DATA IS CURRENT *
 * THROUGH AUGUST 10,1999       *
 *                              *
 *                              *
 ********************************
```

=> s l14

```
      2276 METALLOTH?
     36145 PROMOTER#
      4414 MAMMARY
L15      52 L13(10A)(MAMMARY)
```

=> s l15(10a)(immunoglob? or antibod? or chain#)

```
     11609 IMMUNOGLOB?
     36150 ANTIBOD?
    343081 CHAIN#
L16       1 L15(10A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)
```

=> d

1. 5,733,768, Mar. 31, 1998, Amyloid precursor protein protease; Eric P.
Dixon, et al., 435/226 [IMAGE AVAILABLE]

=> d kwic

US PAT NO: 5,733,768 [IMAGE AVAILABLE] L16: 1 of 1

SUMMARY:

BSUM(64)

The . . . necessary, the appropriate regulatory elements using well known techniques. Promoters which my be used, for example, are the thymidine kinase **promoter**, the **metallothionin** **promoter**, the
heat shock promoter, the mouse **mammary** tumor virus promoter or
various other vital and **immunoglobulin** promoters.

=> s immunoglob? or antibod?

```
     11609 IMMUNOGLOB?
     36150 ANTIBOD?
L17   37141 IMMUNOGLOB? OR ANTIBOD?
```

=> s l17(5)(linked)

MISSING OPERATOR 'L17(5'

=> s l17(5a)(linked)

```
    149754 LINKED
L18    3157 L17(5A)(LINKED)
```

=> s l18(5a)(promoter#)

```
     36145 PROMOTER#
L19      16 L18(5A)(PROMOTER#)
```

=> s l19(5a)(mammary)

```
      4414 MAMMARY
L20       0 L19(5A)(MAMMARY)
```

=> d l19 1- cit ab

1. 5,922,545, Jul. 13, 1999, In vitro peptide and antibody display libraries; Larry C. Mattheakis, et al., 435/6, 5, 7.1; 436/518 [IMAGE AVAILABLE]

US PAT NO: 5,922,545 [IMAGE AVAILABLE] L19: 1 of 16

ABSTRACT:
Improved methods and novel compositions for identifying peptides and
single-chain antibodies that bind to predetermined receptors or epitopes.
Such peptides and antibodies are identified by improved and novel methods
for affinity screening of polysomes displaying nascent peptides.

2. 5,919,452, Jul. 6, 1999, Methods of treating TNF.alpha.-mediated disease using chimeric anti-TNF antibodies; Junming Le, et al., 424/133.1, 145.1, 158.1; 530/387.3, 388.23, 389.2 [IMAGE AVAILABLE]

US PAT NO: 5,919,452 [IMAGE AVAILABLE] L19: 2 of 16

ABSTRACT:
Treatment of tumor necrosis factor, TNF, mediated pathologies is provided
by administering anti-TNF compounds, such as anti-TNF antibodies and
anti-TNF peptides, which compounds are specific for tumor necrosis factor-.alpha. (TNF.alpha.) or tumor necrosis factor-.beta. (TNF.beta.) and which are useful for in vivo therapy or diagnosis of TNF.alpha.-mediated pathologies and conditions, wherein the anti-TNF
compound is selected from the group consisting of at least one of an immunoglobulin variable region, a fragment of a TNF receptor and an anti-TNF peptide, such as a structural analog of a anti-TNF antibody fragment or a TNF receptor fragment.

3. 5,871,901, Feb. 16, 1999, Assay for inhibitors of DP-1 and other DP
proteins; Nicholas Berrie La Thangue, 435/4, 15, 21, 29, 194, 375; 530/358, 388.24, 389.2 [IMAGE AVAILABLE]

US PAT NO: 5,871,901 [IMAGE AVAILABLE] L19: 3 of 16

ABSTRACT:

The protein DP-1, part of the DP-1/E2F-1 transcription factor complex,
as well as DP-2 and DP-3 has its phosphorylation level regulated during
cell cycle progression. This finding allows assays to be based on changes
in phosphorylation of DP proteins, in particular for agents which may
affect the phosphorylation state of DP. DP-1 has been found to have a
greater affinity to DNA when in a hypophosphorylated state. Antibodies
that recognize phosphorylation sites on DP-1 are also disclosed.

4. 5,851,829, Dec. 22, 1998, Method of intracellular binding of target molecules; Wayne A. Marasco, et al., 435/328; 424/577, 578; 435/325, 326,
330, 333, 339, 339.1, 366, 372, 419 [IMAGE AVAILABLE]

US PAT NO: 5,851,829 [IMAGE AVAILABLE] L19: 4 of 16

ABSTRACT:

The present invention relates to a method by which one can target an undesired target molecule or target antigen, preferably a protein. The method comprises the intracellular expression of an antibody capable of
binding to the target. A DNA sequence is delivered to a cell, the DNA sequence contains a sufficient number of nucleotides coding for the portion of an antibody capable of binding to the target operably linked to a promoter that will permit expression of the antibody in the cell(s) of interest. The antibody is then expressed intracellularly and binds to the target, thereby disrupting the target from its normal actions.

5. 5,849,992, Dec. 15, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/14, 7, 15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L19: 5 of 16

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

6. 5,834,597, Nov. 10, 1998, Mutated nonactivating IgG2 domains and anti
CD3 antibodies incorporating the same; J. Yun Tso, et al., 530/387.3 [IMAGE AVAILABLE]

US PAT NO: 5,834,597 [IMAGE AVAILABLE] L19: 6 of 16

ABSTRACT:
The invention provides mutated IgG2 constant regions and anti-CD3 antibodies incorporating the same. Such antibodies specifically bind to the CD3 antigen on T-cells but induce reduced mitogenic response compared
with otherwise identical antibodies bearing natural IgG2 constant regions. The antibodies can be used for treating disorders requiring immune suppression with fewer side effects than result from treatment with prior anti-CD3 antibodies.

7. 5,827,690, Oct. 27, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/7; 530/867 [IMAGE AVAILABLE]

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L19: 7 of 16

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

8. 5,800,815, Sep. 1, 1998, Antibodies to P-selectin and their uses; Robert W. Chestnut, et al., 424/153.1, 133.1, 143.1, 173.1; 435/7.24, 70.21, 326, 328, 343, 346; 530/387.3, 388.2, 388.7, 389.6; 536/23.53 [IMAGE AVAILABLE]

US PAT NO: 5,800,815 [IMAGE AVAILABLE] L19: 8 of 16

ABSTRACT:
The present invention relates to compositions and methods for treating inflammation and other pathological conditions using novel blocking P-selectin antibodies that inhibit adhesion of leukocytes to activated platelets and/or to activated vascular endothelium in vivo. Both murine and humanized antibodies are provided.

9. 5,753,225, May 19, 1998, Antibodies that mimic actions of neurotrophins; Douglas O. Clary, et al., 424/130.1, 141.1, 143.1, 156.1;
530/387.1, 388.1, 388.22 [IMAGE AVAILABLE]

US PAT NO: 5,753,225 [IMAGE AVAILABLE] L19: 9 of 16

ABSTRACT:
The use and production of immunoglobulins which activate trk receptors
and imitate effects of neurotrophins are provided. Immunoglobulins which
block trk receptor activation and methods of use are also provided.

10. 5,714,352, Feb. 3, 1998, Directed switch-mediated DNA recombination;
Aya Jakobovits, 435/462, 320.1, 328, 372.3 [IMAGE AVAILABLE]

US PAT NO: 5,714,352 [IMAGE AVAILABLE] L19: 10 of 16

ABSTRACT:
Switch regions derived from an immunoglobulin (Ig) gene are used to direct recombination between a targeting construct containing a promoter,
a switch region (S.sub.1), and 2) a target locus minimally containing a promoter, a switch region (S.sub.2), and a target sequence.

11. 5,698,195, Dec. 16, 1997, Methods of treating rheumatoid arthritis using chimeric anti-TNF antibodies; Junming Le, et al., 424/133.1, 141.1,
142.1, 145.1; 514/825; 530/351, 387.3, 388.1, 388.23 [IMAGE AVAILABLE]

US PAT NO: 5,698,195 [IMAGE AVAILABLE] L19: 11 of 16

ABSTRACT:
Anti-TNF antibodies, fragments and regions thereof which are specific for
human tumor necrosis factor-.alpha. (TNF.alpha.) and are useful in vivo
for diagnosis and therapy of a number of TNF.alpha.-mediated pathologies
and conditions, including rheumatoid arthritis as well as polynucleotides
coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or
derivative thereof, in immunoassays and immunotherapeutic approaches are
provided.

12. 5,656,272, Aug. 12, 1997, Methods of treating TNF-.alpha.-mediated
Crohn's disease using chimeric anti-TNF antibodies; Junming Le, et al.,
424/133.1, 139.1, 145.1; 435/69.1, 69.6, 69.7; 530/387.3, 388.23 [IMAGE
AVAILABLE]

US PAT NO: 5,656,272 [IMAGE AVAILABLE] L19: 12 of 16

ABSTRACT:
Anti-TNF antibodies, fragments and regions thereof which are specific for
human tumor necrosis factor-.alpha. (TNF.alpha.) and are useful in vivo
for diagnosis and therapy of a number of TNF.alpha.-mediated pathologies
and conditions, including Crohn's disease, as well as polynucleotides
coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or
derivative thereof, in immunoassays and immunotherapeutic

approaches are
provided.

13. 5,635,603, Jun. 3, 1997, Preparation and use of immunoconjugates;
Hans J. Hansen, et al., 530/391.5; 424/172.1; 435/69.6 [IMAGE AVAILABLE]

US PAT NO: 5,635,603 [IMAGE AVAILABLE] L19: 13 of 16

ABSTRACT:
The present invention relates to immunoconjugates comprising an antibody
fragment which is covalently bound to a diagnostic or therapeutic principle through a carbohydrate moiety in the light chain variable region of the antibody fragment. The invention also relates to immunoconjugates comprising an antibody moiety that is an intact antibody
containing a glycosylation site in the light chain variable domain which has been introduced into the antibody by mutating the nucleotide sequence
encoding the light chain. The resultant immunoconjugates retain the immunoreactivity of the antibody fragment or intact antibody, and target
the diagnostic or therapeutic principle to a target tissue where the diagnostic or therapeutic effect is realized. Thus, the invention contemplates the use of such immunoconjugates for diagnosis and immunotherapy. The invention further relates to methods for preparing such immunoconjugates.

14. 5,529,774, Jun. 25, 1996, In vivo transfer of the HSV-TK gene implanted retroviral producer cells; David Barba, et al., 424/93.21, 93.2, 93.6; 514/44 [IMAGE AVAILABLE]

US PAT NO: 5,529,774 [IMAGE AVAILABLE] L19: 14 of 16

ABSTRACT:
The present invention is directed to methods of transferring therapeutic
genes to brain tumor cells in order to kill the cells. In general, the method of the present invention comprises: (1) introducing a retrovirus
containing a selectable marker and at least one gene required for its replication into producer cells such that integration of the proviral DNA
corresponding to the retrovirus into the genome of the producer cell results in the generation of a modified retrovirus wherein at least one of the genes required for replication of the retrovirus is replaced by the therapeutic gene or genes; (2) selecting producer cells in which the modified retrovirus is incorporated as part of the genome of the producer
cells; (3) grafting the producer cells in proximity to the dividing tumor cell in order to infect the tumor cell with the modified retrovirus, thereby transferring the therapeutic gene or genes to the tumor cell; and
(4) killing the cells by administering a substance that is metabolized by the therapeutic gene transferred to the tumor cells into a metabolite that kills the cells. Suitable retroviral vectors and methods for generating them, producer cells, and grafting methods are described.

15. 5,474,771, Dec. 12, 1995, Murine monoclonal antibody (5c8) recognizes a human glycoprotein on the surface of T-lymphocytes, compositions containing same; Seth Lederman, et al., 424/133.1, 130.1,
144.1, 153.1, 154.1; 435/70.21, 343.2; 530/388.7, 388.73, 388.75 [IMAGE
AVAILABLE]

US PAT NO: 5,474,771 [IMAGE AVAILABLE] L19: 15 of 16

ABSTRACT:
This invention provides a monoclonal antibody which specifically recognizes and forms a complex with a protein located on the surface of
activated T cells and thereby inhibits T cell activation of B cells. This invention also provides the monoclonal antibody 5c8 (ATCC Accession No.
HB 10916).
This invention provides a human CD4.sup.- T cell leukemia cell line designated D1.1 (ATCC Accession No. CRL 10915) capable of constitutively
providing contact-dependent helper function to B cells. This invention also provides an isolated protein from the surface of activated T cells, wherein the protein is necessary for T cell activation of B cells. This invention further provides an isolated, soluble protein from the surface of activated T cells, wherein the protein is necessary for T cell activation of B cells.

16. 5,443,953, Aug. 22, 1995, Preparation and use of immunoconjugates;
Hans J. Hansen, et al., 424/1.49, 1.53, 9.341, 178.1, 179.1, 180.1, 181.1, 182.1, 183.1; 435/7.1, 7.2, 7.23, 69.6; 530/387.3, 391.3, 391.5, 391.7, 391.9 [IMAGE AVAILABLE]

US PAT NO: 5,443,953 [IMAGE AVAILABLE] L19: 16 of 16

ABSTRACT:
The present invention relates to immunoconjugates comprising an antibody
fragment which is covalently bound to a diagnostic or therapeutic principle through a carbohydrate moiety in the light chain variable region of the antibody fragment. The invention also relates to immunoconjugates comprising an antibody moiety that is an intact antibody
containing a glycosylation site in the light chain variable domain which has been introduced into the antibody by mutating the nucleotide sequence
encoding the light chain. The resultant immunoconjugates retain the immunoreactivity of the antibody fragment or intact antibody, and target
the diagnostic or therapeutic principle to a target tissue where the diagnostic or therapeutic effect is realized. Thus, the invention contemplates the use of such immunoconjugates for diagnosis and immunotherapy. The invention further relates to methods for preparing such immunoconjugates.

=> d his

(FILE 'USPAT' ENTERED AT 09:28:32 ON 10 AUG 1999)
L1 1307 S MAMMARY TUMOR
L2 202 S L1(5A)(PROMOTER)
L3 1 S L2(10A)(ANTIBOD? OR IMMUNOGLOBULIN#)
L4 299 S MAMMARY(5A)(PROMOTER#)
L5 3 S L4(10A)(ANTIBOD? OR IMMUNOGLOB? OR CHAIN#)
L6 888 S MOUSE MAMMARY
L7 210 S L6(5A)(PROMOTER#)
L8 1 S L7(5A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)
L9 74 S TUMOR VIRUS PROMOTER#
L10 74 S L9(5A)(MAMMARY)
L11 1 S L10(10A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)

FILE 'EPOABS' ENTERED AT 09:36:47 ON 10 AUG 1999
L12 0 S L11
L13 13 S (METALLOTH?)(3A)(PROMOTER#)
L14 0 S L13(10A)(MAMMARY)

FILE 'USPAT' ENTERED AT 09:37:55 ON 10 AUG 1999
L15 52 S L14
L16 1 S L15(10A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)
L17 37141 S IMMUNOGLOB? OR ANTIBOD?
L18 3157 S L17(5A)(LINKED)
L19 16 S L18(5A)(PROMOTER#)
L20 0 S L19(5A)(MAMMARY)

=> s l17(5a)(recombinant)

21367 RECOMBINANT
L21 2752 L17(5A)(RECOMBINANT)

=> s l17(3a)(recombinant)

21367 RECOMBINANT
L22 2094 L17(3A)(RECOMBINANT)

=> s l22(5a)(construct# or plasmid# or vector#)

96626 CONSTRUCT#
16628 PLASMID#
77567 VECTOR#
L23 84 L22(5A)(CONSTRUCT# OR PLASMID# OR VECTOR#)

=> s l23(5a)(promoter#)

36145 PROMOTER#
L24 0 L23(5A)(PROMOTER#)

=> s l23 and mammary

4414 MAMMARY
L25 9 L23 AND MAMMARY

=> d 1- cit ab

1. 5,912,160, Jun. 15, 1999, Gabl, Grb2 binding protein, and compositions for making and methods of using the same; Albert J. Wong, et
al., 435/252.3, 69.1, 320.1; 530/350; 536/23.5, 24.3 [IMAGE AVAILABLE]

US PAT NO: 5,912,160 [IMAGE AVAILABLE] L25: 1 of 9

ABSTRACT:
A substantially pure protein, Gabl, that binds to Grb2 is disclosed. Isolated nucleic acid molecules that encode Gabl is disclosed. Pharmaceutical compositions comprising a pharmaceutically acceptable
carrier in combination with nucleic acid molecules are disclosed. Fragments of nucleic acid molecules that encode Gabl having at least 10
nucleotides and oligonucleotide molecule comprising a nucleotide sequence
complimentary to a nucleotide sequence of at least 10 nucleotides are disclosed. Recombinant expression vectors that comprise the nucleic acid
molecule that encode Gabl, and host cells that comprise such **recombinant** **vectors** are disclosed. **Antibodies** that bind to an
epitope on Gabl are disclosed. Methods of identifying inhibitors, activators and substrates of Gabl are disclosed. Antisense compounds and
methods of using the same are disclosed.

2. 5,880,268, Mar. 9, 1999, Modulators of the interaction between ICAM-R
and .alpha..sub.d /CD18; W. Michael Gallatin, et al., 530/387.3, 387.9, 388.1, 388.22 [IMAGE AVAILABLE]

US PAT NO: 5,880,268 [IMAGE AVAILABLE] L25: 2 of 9

ABSTRACT:
DNA sequences encoding a novel human intercellular adhesion molecule
polypeptide (designated "ICAM-R") and variants thereof are disclosed along with methods and materials for production of the same by recombinant procedures. Binding molecules specific for ICAM-R and variants thereof are also disclosed as useful in both the isolation of ICAM-R from natural cellular sources and the modulation of ligand/receptor binding biological activities of ICAM-R. Specifically, antibody substances which modulate the interaction between ICAM-R and
ad/CD18 are provided.

3. 5,869,262, Feb. 9, 1999, Method for monitoring an inflammatory disease state by detecting circulating ICAM-R; W. Michael Gallatin, et
al., 435/7.1, 7.92, 7.94, 7.95; 436/811 [IMAGE AVAILABLE]

US PAT NO: 5,869,262 [IMAGE AVAILABLE] L25: 3 of 9

ABSTRACT:
Methods for monitoring the progression of systemic lupus erythematosus
(SLE) in a patient by detecting elevated levels of circulating ICAM-R wherein progression is indicated in an SLE patient whose circulating ICAM-R levels are increased as compared to normal individuals or individuals with in active SLE. Methods for the detection of an inflammatory disease state selected from the group consisting of rheumatoid arthritis, SLE, and Guillain-Barre syndrome and multiple sclerosis in a patient by detecting elevated levels of circulating ICAM-R
wherein the presence of the inflammatory disease state is indicated in a
patient whose circulating ICAM-R levels are increased as compared to normal healthy individuals. ICAM-R is also known as ICAM-3 and CDw50 in
the art.

4. 5,837,822, Nov. 17, 1998, Humanized antibodies specific for ICAM
related protein; W. Michael Gallatin, et al., 530/387.3, 388.1, 388.22 [IMAGE AVAILABLE]

US PAT NO: 5,837,822 [IMAGE AVAILABLE] L25: 4 of 9

ABSTRACT:
DNA sequences encoding a novel human intercellular adhesion molecule
polypeptide (designated "ICAM-R") and variants thereof are disclosed along with methods and materials for production of the same by recombinant procedures. Binding molecules specific for ICAM-R and variants thereof are also disclosed as useful in both the isolation of ICAM-R from natural cellular sources and the modulation of ligand/receptor binding biological activities of ICAM-R. More specifically, humanized antibodies specific for ICAM-R proteins are disclosed.

5. 5,811,517, Sep. 22, 1998, ICAM-related protein variants; W. Michael
Gallatin, et al., 530/350; 435/69.1, 69.7, 252.3, 320.1, 325; 536/23.1, 23.4 [IMAGE AVAILABLE]

US PAT NO: 5,811,517 [IMAGE AVAILABLE] L25: 5 of 9

ABSTRACT:
DNA sequences encoding a novel human intercellular adhesion molecule
polypeptide (designated "ICAM-R") and variants thereof are disclosed along with methods and materials for production of the same by recombinant procedures. Binding molecules specific for ICAM-R and variants thereof are also disclosed as useful in both the isolation of ICAM-R from natural cellular sources and the modulation of ligand/receptor binding biological activities of ICAM-R.

6. 5,773,218, Jun. 30, 1998, Method to identify compounds which modulate
ICAM-related protein interactions; W. Michael Gallatin, et al., 435/6 [IMAGE AVAILABLE]

US PAT NO: 5,773,218 [IMAGE AVAILABLE] L25: 6 of 9

ABSTRACT:
DNA sequences encoding a novel human intercellular adhesion molecule
polypeptide (designated "ICAM-R") and variants thereof are disclosed along with methods and materials for production of the same by recombinant procedures. Binding molecules specific for ICAM-R and variants thereof are also disclosed as useful in both the isolation of ICAM-R from natural cellular sources and the modulation of ligand/receptor binding biological activities of ICAM-R.

7. 5,672,500, Sep. 30, 1997, Mch2, an apoptotic cysteine protease, and
compositions for making and methods of using the same; Gerald Litwack, et
al., 435/252.3, 320.1; 530/350; 536/23.2 [IMAGE AVAILABLE]

US PAT NO: 5,672,500 [IMAGE AVAILABLE] L25: 7 of 9

ABSTRACT:
A substantially pure protein that is a member of the apoptotic Ced-3/Ice
cysteine protease gene family, Mch2.alpha., and an inactive isoform of it, Mch2.beta., are disclosed. Isolated nucleic acid molecules that encode Mch2.alpha. and Mch2.beta., respectively, are disclosed. Pharmaceutical compositions comprising a pharmaceutically acceptable
carrier in combination with the protein or the nucleic acid molecules are
disclosed. Fragments of nucleic acid molecules that encode Mch2.alpha.
and Mch2.beta. having at least 10 nucleotides and oligonucleotide molecule comprising a nucleotide sequence complimentary to a nucleotide
sequence of at least 10 nucleotides are disclosed. Recombinant

expression
vectors that comprise the nucleic acid molecule that encode Mch2.alpha.
or Mch2.beta., and host cells that comprise such **recombinant** **vectors** are disclosed. **Antibodies** that bind to an epitope on Mch2.alpha. and/or Mch2.beta. are disclosed. Methods of identifying inhibitors, activators and substrates of Mch2.alpha. are disclosed. Antisense compounds and methods of using the same are disclosed.

8. 5,631,133, May 20, 1997, Transition in transcriptional activation by intracellular hormone receptors at the tumor stage of dermal fibrosarcoma
development; Douglas Hanahan, et al., 435/6, 69.4 [IMAGE AVAILABLE]

US PAT NO: 5,631,133 [IMAGE AVAILABLE] L25: 8 of 9

ABSTRACT:
Intracellular hormone receptors are discovered to undergo posttranslational regulation. Assays to assess cancer progression and to permit discovery of a new class of biologically active compounds are provided. Related kits are also provided.

9. 5,571,894, Nov. 5, 1996, Recombinant antibodies specific for a growth
factor receptor; Winfried S. Wels, et al., 530/387.3; 435/69.1; 530/350;
536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,571,894 [IMAGE AVAILABLE] L25: 9 of 9

ABSTRACT:
The invention concerns recombinant antibodies directed to the extracellular domain of the human growth factor receptor c-erbB-2 comprising a light chain variable domain and a heavy chain variable domain of a monoclonal antibody, monoclonal antibodies directed to c-erbB-2 themselves, a method of manufacturing those recombinant and
monoclonal antibodies, hybridoma cells secreting those monoclonal antibodies, a method of manufacturing those hybridoma cells, DNAs encoding the heavy and light chain variable domains and the recombinant
antibody, a method of manufacturing that DNA, hybrid vectors suitable for
the expression of that DNA, host cells transformed with that DNA, and
processes of using those recombinant and monoclonal antibodies in the diagnosis and treatment of tumors.

=> d 9 kwic

US PAT NO: 5,571,894 [IMAGE AVAILABLE] L25: 9 of 9

SUMMARY:

BSUM(112)

The . . . either sequentially or simultaneously, or by using a vector construct comprising both the L-chain and H-chain genes, for example a
recombinant single-chain **antibody** gene **construct** as indicated
hereinbefore.

SUMMARY:

BSUM(113)

Preferred are host cells transformed with a **recombinant** single-chain
antibody gene **construct** comprising DNA coding for the heavy chain
variable domain of an anti-c-erbB-2 antibody, DNA coding for a spacer group, DNA. . . . chain variable domain of an anti-c-erbB-2 antibody and
DNA coding for an effector molecule, in particular transfected with the preferred **recombinant** single-chain **antibody** gene
construct as
indicated hereinbefore. Further examples of host cells of the invention are cells transferred with similar recombinant plasmids which contain.
.
.

DETDESC:

DETD(7)

1.3.1 . . . immunofluorescent staining of mouse cells expressing high levels of the human c-erbB-2 protein. To isolate these cells the HC11 mouse **mammary** epithelial cell line (Ball at al., EMBO J. 7: 2089,
1988) is transfected according to conventional, previously described methods (Graham. . .

DETDESC:

DETD(124)

15.1 Immunotoxin treatment of cell lines: Human breast and ovarian tumor
cell lines SK-BR3, MDAMB-231, MDA-MB-453, HTB77, the mouse **mammary**
epithelial cell line HC11, and HC11 cells transfected with the human c-erbB-2 cDNA are plated on 48 well tissue culture. . .

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(FILE 'USPAT' ENTERED AT 09:28:32 ON 10 AUG 1999)
L1 1307 S MAMMARY TUMOR
L2 202 S L1(5A)(PROMOTER)
L3 1 S L2(10A)(ANTIBOD? OR IMMUNOGLOBULIN#)
L4 299 S MAMMARY(5A)(PROMOTER#)
L5 3 S L4(10A)(ANTIBOD? OR IMMUNOGLOB? OR CHAIN#)
L6 888 S MOUSE MAMMARY
L7 210 S L6(5A)(PROMOTER#)
L8 1 S L7(5A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)
L9 74 S TUMOR VIRUS PROMOTER#
L10 74 S L9(5A)(MAMMARY)
L11 1 S L10(10A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)

FILE 'EPOABS' ENTERED AT 09:36:47 ON 10 AUG 1999
L12 0 S L11
L13 13 S (METALLOTH?)(3A)(PROMOTER#)
L14 0 S L13(10A)(MAMMARY)

FILE 'USPAT' ENTERED AT 09:37:55 ON 10 AUG 1999
L15 52 S L14
L16 1 S L15(10A)(IMMUNOGLOB? OR ANTIBOD? OR CHAIN#)
L17 37141 S IMMUNOGLOB? OR ANTIBOD?
L18 3157 S L17(5A)(LINKED)
L19 16 S L18(5A)(PROMOTER#)
L20 0 S L19(5A)(MAMMARY)
L21 2752 S L17(5A)(RECOMBINANT)
L22 2094 S L17(3A)(RECOMBINANT)
L23 84 S L22(5A)(CONSTRUCT# OR PLASMID# OR VECTOR#)
L24 0 S L23(5A)(PROMOTER#)
L25 9 S L23 AND MAMMARY

=> s antibod? or immunoglobul?

36150 ANTIBOD?
11437 IMMUNOGLOBUL?
L26 37116 ANTIBOD? OR IMMUNOGLOBUL?

=> s l26(10a)milk

29073 MILK
L27 721 L26(10A)MILK

=> s l26(5a)milk

29073 MILK
L28 393 L26(5A)MILK

=> s l28(10a)(recombinant)

21367 RECOMBINANT
L29 8 L28(10A)(RECOMBINANT)

=> d 1- cit ab

1. 5,849,992, Dec. 15, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/14, 7, 15, 16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,849,992 [IMAGE AVAILABLE] L29: 1 of 8

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

2. 5,827,690, Oct. 27, 1998, Transgenic production of antibodies in milk; Harry Meade, et al., 800/7; 530/867 [IMAGE AVAILABLE]

US PAT NO: 5,827,690 [IMAGE AVAILABLE] L29: 2 of 8

ABSTRACT:
A method for the production of monoclonal antibodies in mammal's milk,
through the creation of transgenic animals that selectively express foreign antibody genes in mammary epithelial cells.

3. 5,827,683, Oct. 27, 1998, Nucleic acids encoding BSSL variants; Lars
Gustav Blackberg, et al., 435/69.1, 69.7, 70.1, 70.3, 71.1, 200, 243, 320.1, 325; 536/23.1, 23.2, 23.5 [IMAGE AVAILABLE]

US PAT NO: 5,827,683 [IMAGE AVAILABLE] L29: 3 of 8

ABSTRACT:
The invention discloses nucleic acids encoding variant Bile Salt Stimulated Lipase (BSSL; EC 3.1.1.1). The encoded variant BSSL enzymes
maintain catalytic activity but contain fewer glycosylation sites that full-length BSSL. This reduced glycosylation facilitates purification and
characterization of recombinant BSSL proteins.

4. 5,763,739, Jun. 9, 1998, Transgenic non-human mammals producing BSSL
variants; Lars Gustav Blackberg, et al., 800/18; 435/69.1; 800/7, 14, 15,
16, 17, 21, 25 [IMAGE AVAILABLE]

US PAT NO: 5,763,739 [IMAGE AVAILABLE] L29: 4 of 8

ABSTRACT:
The present invention relates to novel polypeptides which are variants of
Bile Salt-Stimulated Lipase (BSSL; EC 3.1.1.1). It also relates to DNA
molecules encoding the said polypeptides, and to subproducts comprising
the said DNA molecules. The invention further relates to processes for producing the said BSSL variants and for producing transgenic non-human
mammals capable of expressing the BSSL variants.
Furthermore the invention relates to such transgenic animals as well as to infant formulas comprising milk from such transgenic animals. The invention also relates to pharmaceutical compositions comprising the said
polypeptides; and the use of the said polypeptides and DNA molecules for
the manufacture of medicaments.

5. 5,750,172, May 12, 1998, Transgenic non human mammal milk; Harry
Meade, et al., 426/580; 435/69.1, 69.4, 69.51, 69.52, 69.6, 183, 215; 800/7 [IMAGE AVAILABLE]

US PAT NO: 5,750,172 [IMAGE AVAILABLE] L29: 5 of 8

ABSTRACT:
This invention relates to the production of recombinant proteins, such as
coagulation factors VIII and IX, tissue plasminogen activator (TPA), urokinase, growth hormone, insulin, interferons, interleukins, peptide hormones and immunoglobulins, in mammals' milk. Particularly, this invention relates to an expression system which when transgenically incorporated into a mammal permits the female species of that mammal to
produce the desired recombinant protein in or along with its milk. This invention also relates to the transgenic mammal that produces the desired
recombinant product in its milk.

6. 5,728,560, Mar. 17, 1998, Method of treating CD4+ T cell lymphopenia
in immuno-compromised patients; Robert G. L. Shorr, et al., 435/103, 188,
227; 514/4, 21, 46 [IMAGE AVAILABLE]

US PAT NO: 5,728,560 [IMAGE AVAILABLE] L29: 6 of 8

ABSTRACT:
The present invention is directed to methods of treating CD4+ T cell lymphopenia in HIV-infected patients. The methods include administering
an effective mount of adenosine deaminase or related enzymatic material
to a patient in need thereof. In preferred aspects of the invention, the method is employed in conjunction with HIV-infected patients having CD4+
T cell levels of less than about 200/.mu.l. Effective amounts of the enzyme range from about 5 to about 50 IU/kg/week. In one particularly
preferred aspect of the invention, the adenosine deaminase is conjugated
to one or more strands of polyethylene glycol to prolonged activity in vivo.

7. 5,691,135, Nov. 25, 1997, Immunoglobulin superantigen binding to gp
120 from HIV; Jonathan Braun, et al., 435/5, 7.1, 7.2, 7.24, 7.92, 974 [IMAGE AVAILABLE]

US PAT NO: 5,691,135 [IMAGE AVAILABLE] L29: 7 of 8

ABSTRACT:
VH3 and VH4 type immunoglobulins display superantigen-type binding
affinity for the HIV gp120 envelope glycoprotein. VH3 and VH4 type antibody molecules, including IgG and IgM, are shown to suppress HIV
infection in vivo and in vitro. Determining the level of such antibody molecules is correlated to the advancement of HIV disease state.

8. 4,873,316, Oct. 10, 1989, Isolation of exogenous recombinant proteins
from the milk of transgenic mammals; Harry Meade, et al., 800/7; 435/69.1, 69.2, 69.4, 69.5, 69.6, 69.8; 530/360, 361, 416, 417, 418, 832,
833; 536/23.1, 23.4, 23.5; 800/18 [IMAGE AVAILABLE]

US PAT NO: 4,873,316 [IMAGE AVAILABLE] L29: 8 of 8

ABSTRACT:
This invention relates to the production of recombinant proteins in mammals' milk. Particularly, this invention relates to an expression system comprising the mammal's casein promoter which when transgenically
incorporated into a mammal permits the female species of that mammal to
produce the desired recombinant protein in or along with its milk. This invention also relates to the transgenic mammal that produces the desired
recombinant product in its milk.

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(FILE 'USPAT' ENTERED AT 09:28:32 ON 10 AUG 1999)
L1 1307 S MAMMARY TUMOR
L2 202 S L1(5A)(PROMOTER)
L3 1 S L2(10A)(ANTIBOD? OR IMMUNOGLOBULIN#)
L4 299 S MAMMARY(5A)(PROMOTER#)
L5 3 S L4(10A)(ANTIBOD? OR IMMUNOGLOB? OR CHAIN#)
L6 888 S MOUSE MAMMARY
L7 210 S L6(5A)(PROMOTER#)
L8 1 S L7(5A)(IMMUNOGLOB? OR ANTIBOD? OR

CHAIN#)
L9 74 S TUMOR VIRUS PROMOTER#
L10 74 S L9(5A)(MAMMARY)
L11 1 S L10(10A)(IMMUNOGLOB? OR ANTIBOD? OR
CHAIN#)

FILE 'EPOABS' ENTERED AT 09:36:47 ON 10 AUG 1999
L12 0 S L11
L13 13 S (METALLOTH?)(3A)(PROMOTER#)
L14 0 S L13(10A)(MAMMARY)

FILE 'USPAT' ENTERED AT 09:37:55 ON 10 AUG 1999
L15 52 S L14
L16 1 S L15(10A)(IMMUNOGLOB? OR ANTIBOD? OR
CHAIN#)
L17 37141 S IMMUNOGLOB? OR ANTIBOD?
L18 3157 S L17(5A)(LINKED)
L19 16 S L18(5A)(PROMOTER#)
L20 0 S L19(5A)(MAMMARY)
L21 2752 S L17(5A)(RECOMBINANT)
L22 2094 S L17(3A)(RECOMBINANT)
L23 84 S L22(5A)(CONSTRUCT# OR PLASMID# OR
VECTOR#)
L24 0 S L23(5A)(PROMOTER#)
L25 9 S L23 AND MAMMARY
L26 37116 S ANTIBOD? OR IMMUNOGLOBUL?
L27 721 S L26(10A)MILK
L28 393 S L26(5A)MILK
L29 8 S L28(10A)(RECOMBINANT)

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U.S. Patent & Trademark Office LOGOFF AT 09:50:37 ON 10 AUG
1999

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FILE 'USPAT' ENTERED AT 16:02:55 ON 06 AUG 1999

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 *    U.S. PATENT TEXT FILE     *
 *                              *
 * THE WEEKLY PATENT TEXT AND IMAGE DATA IS
CURRENT      *
 * THROUGH AUGUST 3,1999                *
 *                              *
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=> s immunoglobulin#(10a)(construct#)

      11365 IMMUNOGLOBULIN#
      96404 CONSTRUCT#
L1      139 IMMUNOGLOBULIN#(10A)(CONSTRUCT#)

=> s immunoglobulin#(5a)(construct#)

      11365 IMMUNOGLOBULIN#
      96404 CONSTRUCT#
L2       90 IMMUNOGLOBULIN#(5A)(CONSTRUCT#)

=> s l2(10a)(light chain)

     679503 LIGHT
     318197 CHAIN
       2289 LIGHT CHAIN
            (LIGHT(W)CHAIN)
L3        5 L2(10A)(LIGHT CHAIN)

=> s l3(10a)(heavy chain)

     226973 HEAVY
     318197 CHAIN
       2515 HEAVY CHAIN
            (HEAVY(W)CHAIN)
L4        4 L3(10A)(HEAVY CHAIN)

=> d 1- cit ab
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1. 5,891,717, Apr. 6, 1999, Methods and compositions for inhibiting hexokinase; Christopher B. Newgard, et al., 435/325, 69.1, 69.7, 194, 320.1, 455, 456, 458, 463; 536/23.2, 23.4 [IMAGE AVAILABLE]

US PAT NO: 5,891,717 [IMAGE AVAILABLE] L4: 1 of 4

ABSTRACT:
Disclosed are compositions and methods for inhibiting hexokinase enzymes
in mammalian cells. Specifically provided are proteins that stimulate the
production of trehalose-6-phosphate and their respective genes; hexokinase-specific ribozymes and genes encoding such constructs; and
agents that competitively reduce hexokinase activity, e.g., by displacing
hexokinase from mitochondria, and their respective genes. The latter group of agents includes inactive hexokinases and fragments thereof that
retain mitochondrial binding functions and hexokinase-glucokinase chimeras that further substitute glucokinase activity for hexokinase activity. Mammalian cells including such hexokinase inhibitors, methods
of making such cells and various in vitro and in vivo methods of using cells with reduced hexokinase activity are also described herein.

2. 5,854,067, Dec. 29, 1998, Hexokinase inhibitors; Christopher B. Newgard, et al., 435/366, 4, 6, 91.1, 91.31, 183, 320.1, 325; 536/23.1, 24.31, 24.5 [IMAGE AVAILABLE]

US PAT NO: 5,854,067 [IMAGE AVAILABLE] L4: 2 of 4

ABSTRACT:
Disclosed are compositions and methods for inhibiting hexokinase enzymes
in mammalian cells. Specifically provided are proteins that stimulate the
production of trehalose-6-phosphate and their respective genes; hexokinase-specific ribozymes and genes encoding such constructs; and
agents that competitively reduce hexokinase activity, e.g., by displacing
hexokinase from mitochondria, and their respective genes. The latter group of agents includes inactive hexokinases and fragments thereof that
retain mitochondrial binding functions and hexokinase-glucokinase chimeras that further substitute glucokinase activity for hexokinase activity. Mammalian cells including such hexokinase inhibitors, methods
of making such cells and various in vitro and in vivo methods of using cells with reduced hexokinase activity are also described herein.

3. 5,786,213, Jul. 28, 1998, Inhibition of endogenous gastrin expression
for treatment of colorectal cancer; Pomila Singh, et al., 435/320.1; 424/93.21; 435/69.1, 325; 514/2, 44; 536/23.1, 24.3 [IMAGE AVAILABLE]

US PAT NO: 5,786,213 [IMAGE AVAILABLE] L4: 3 of 4

ABSTRACT:
The present invention discloses is for the treatment of colon cancer. The
expression of gastrin by colon cancers is inhibited by the use of antisense gastrin expression. Methods are disclosed for the preparation of expression constructs and the use of such constructs to inhibit colon cancer growth.

4. 5,610,034, Mar. 11, 1997, Immunoglobulin production by trichoderma;
Eini Nyyssonen, et al., 435/69.6, 69.8, 254.6, 320.1, 484; 536/23.53, 24.1 [IMAGE AVAILABLE]

US PAT NO: 5,610,034 [IMAGE AVAILABLE] L4: 4 of 4

ABSTRACT:
Methods for the production of recombinant immunoglobulins in a Trichoderma host are described.

For

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=> s l2(p)(assembl?)

     807526 ASSEMBL?
L5        6 L2(P)(ASSEMBL?)

=> d 1- cit ab
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1. 5,831,036, Nov. 3, 1998, Soluble fragments of human intercellular adhesion molecule-1; Timothy A. Springer, et al., 530/395; 424/185.1; 435/69.3; 530/300, 350 [IMAGE AVAILABLE]

US PAT NO: 5,831,036 [IMAGE AVAILABLE] L5: 1 of 6

ABSTRACT:
The present invention relates to intercellular adhesion molecules (ICAM-1) which are involved in the process through which lymphocytes
recognize and migrate to sites of inflammation as well as attach to cellular substrates during inflammation. The invention is directed toward
such molecules, screening assays for identifying such molecules and antibodies capable of binding such molecules. The invention also includes
uses for adhesion molecules and for the antibodies that are capable of binding them.

2. 5,639,947, Jun. 17, 1997, Compositions containing glycopolypeptide
multimers and methods of making same in plants; Andrew C. Hiatt, et al.,
800/267; 435/69.6; 530/387.1, 387.3; 536/23.53; 800/288, 298 [IMAGE
AVAILABLE]

US PAT NO: 5,639,947 [IMAGE AVAILABLE] L5: 2 of 6

ABSTRACT:
The present invention contemplates a transgenic plant having somatic and
germ cells containing at least two mammalian genes coding for polypeptides capable of autogenously associating with each other to form
a biologically active multimer. In addition, the invention describes a method for producing a glycopolypeptide multimer by introducing first

and
second mammalian genes encoding the constituent parts of the multimer
into first and second respective members of a plant species, generating a
progeny from the first and second plant species members, and isolating the glycopolypeptide multimer from the progeny plant.

3. 5,612,216, Mar. 18, 1997, Nucleotide sequence encoding intercellular
adhesion molecule-1 and fragments thereof; Timothy A. Springer, et al.,
435/252.3, 69.1, 320.1; 530/395; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,612,216 [IMAGE AVAILABLE] L5: 3 of 6

ABSTRACT:
The present invention relates to intercellular adhesion molecules (ICAM-1) which are involved in the process through which lymphocytes
recognize and migrate to sites of inflammation as well as attach to cellular substrates during inflammation. The invention is directed toward
such molecules, screening assays for identifying such molecules and antibodies capable of binding such molecules. The invention also includes
uses for adhesion molecules and for the antibodies that are capable of binding them.

4. 5,475,091, Dec. 12, 1995, R6-5-D6, an antibody which binds intercellular adhesion molecule-1; Timothy A. Springer, et al.,
530/388.22, 388.85, 389.2 [IMAGE AVAILABLE]

US PAT NO: 5,475,091 [IMAGE AVAILABLE] L5: 4 of 6

ABSTRACT:
The present invention relates to intercellular adhesion molecules (ICAM-1) which are involved in the process through which lymphocytes
recognize and migrate to sites of inflammation as well as attach to cellular substrates during inflammation. The invention is directed toward
such molecules, screening assays for identifying such molecules and antibodies capable of binding such molecules. The invention also includes
uses for adhesion molecules and for the antibodies that are capable of binding them.

5. 5,284,931, Feb. 8, 1994, Intercellular adhesion molecules, and their binding ligands; Timothy A. Springer, et al., 424/139.1, 152.1, 153.1, 154.1, 172.1, 173.1; 514/8; 530/388.22, 395, 808, 868 [IMAGE AVAILABLE]

US PAT NO: 5,284,931 [IMAGE AVAILABLE] L5: 5 of 6

ABSTRACT:
Pharmaceutical compositions comprising antibodies to intercellular adhesion molecule-1 (ICAM-1 or CD54) are useful in methods of decreasing
the severity of inflammation associated with the adhesion of leukocytes
to cells bearing ICAM-1. Treatment with anti-ICAM-1 antibodies reduced
the severity of inflammation associated with acute organ or tissue rejection and prolonged allograft survival time. Such compositions may
optionally contain other immunsuppressive agents.

6. 5,202,422, Apr. 13, 1993, Compositions containing plant-produced glycopolypeptide multimers, multimeric proteins and method of their use;
Andrew C. Hiatt, et al., 424/132.1, 133.1, 150.1, 804; 435/69.6, 70.21, 188.5, 252.3, 320.1; 530/387.1, 387.3, 388.1, 388.4, 861; 800/288 [IMAGE
AVAILABLE]

US PAT NO: 5,202,422 [IMAGE AVAILABLE] L5: 6 of 6

ABSTRACT:
The present invention contemplates glycopolypeptide multimers having a
polypeptide that contain an immunoglobulin amino acid residue sequence
and an oligosaccharide that comprises a core pentasaccharide and N-acetylglucosamine-containing outer branches, such that the multimer is
free from sialic acid. The production of passive immunity in an animal by
administering a sialic acid free glycopolypeptide multimer is also contemplated. In addition, the invention describes a method for producing
a glycopolypeptide multimer by introducing first and second mammalian
genes encoding the constituent parts of the multimer into first and second respective members of a plant species, generating a progeny from
the first and second plant species members, and isolating the glycopolypeptide multimer from the progeny plant.

=> s (immunoglobulin# or antibod?)(10a)(sequence#)

11365 IMMUNOGLOBULIN#
36023 ANTIBOD?
366097 SEQUENCE#
L6 5358 (IMMUNOGLOBULIN# OR ANTIBOD?)(10A)(SEQUENCE#)

=> s l6 and (assemb? or function?)

807563 ASSEMB?
1160058 FUNCTION?
L7 4899 L6 AND (ASSEMB? OR FUNCTION?)

=> s l6(10a)(assemb? or function?)

807563 ASSEMB?
1160058 FUNCTION?
L8 292 L6(10A)(ASSEMB? OR FUNCTION?)

=> d 280- cit ab

280. 4,935,496, Jun. 19, 1990, Mouse-human chimaeric immunoglobulin
heavy chain specific for the call antigen; Akira Kudo, et al., 530/387.3, 388.15, 388.73, 388.75, 808, 809, 828, 866, 867 [IMAGE AVAILABLE]

US PAT NO: 4,935,496 [IMAGE AVAILABLE] L8: 280 of 292

ABSTRACT:
A mouse-human chimaeric immunoglobulin heavy chain comprising (a) the
amino acid sequence of a mouse immunoglobulin heavy chain variable region
and (b) the amino acid sequence of a human immunoglobulin heavy chain
constant region and reacting specifically with human common acute lympohocytic leukemia antigen and a chimaeric DNA fragment which encodes
the amino acid sequence of the above mouse-human chimaeric immunoglobulin
heavy chain.

281. 4,920,213, Apr. 24, 1990, Method and compositions useful in preventing equine influenza; Beverly Dale, et al., 536/23.72; 435/69.1, 69.3, 200, 201, 235.1, 320.1; 536/23.2, 23.7 [IMAGE AVAILABLE]

US PAT NO: 4,920,213 [IMAGE AVAILABLE] L8: 281 of 292

ABSTRACT:
Recombinant vaccines for immunizing horses against equine influenza virus
(EIV) are disclosed. The DNA sequences encoding the hemagglutinin (HA)
and neuraminidase (NA) glycoproteins from the two strains of EIV currently infective in horses are used to construct vaccinia carried vaccines, to design synthetic peptides for primer and booster administration, and to permit recombinant synthesis of HA and/or NA protein based vaccines. These DNA sequences also provide probes useful
for preparing similar vaccines from fresh isolates of new strains generated by genetic drift.

282. 4,906,564, Mar. 6, 1990, Antigenic determinants recognized by antibodies obtained using a pathogenic agent or a derivative thereof that
presents a restricted set of antigens; Jeffery A. Lyon, et al., 435/7.22,

5, 29; 530/350, 388.6, 412, 413 [IMAGE AVAILABLE]

US PAT NO: 4,906,564 [IMAGE AVAILABLE] L8: 282 of 292

ABSTRACT:
A method provides peptides that are antigenic determinants identified by
antibodies obtained using intact pathogenic agents that present a restricted set of antigens to surveillance by the immune system.

283. 4,906,562, Mar. 6, 1990, Monocolonal antibodies and antigen for human non-small cell lung carcinomas; Ingegerd Hellstrom, et al., 435/7.23, 188; 436/514, 537, 542, 547, 548; 530/387.5, 388.8, 806, 808,
828, 866 [IMAGE AVAILABLE]

US PAT NO: 4,906,562 [IMAGE AVAILABLE] L8: 283 of 292

ABSTRACT:
The present invention is concerned with novel monoclonal antibodies which
define a glycolipid antigen associated with human non-small cell lung carcinomas ("NSCLC") and certain other human carcinomas. The antibodies
bind to normal human cells to a much lesser degree than to tumor cells.
The antibodies find use in diagnostic methods such as the detection of malignant cells associated with NSCLC and in therapeutic methods. Also
disclosed in a novel glycolipid antigen. The invention also comprises a method for determining the presence of a malignant condition in lung tissue and other human tissue. The method involves examining the human
tissue for the presence of a glycolipid antigen having the terminal carbohydrate sequence:
GalNAc.beta.l.fwdarw.4Gal.beta.l.fwdarw.3GalNAc.be
ta.l.fwdarw.4Gal.beta.l.fwdarw.R.

284. 4,889,802, Dec. 26, 1989, Enhanced production of recombinant proteins in myeloma cells; Tristram G. Parslow, et al., 435/69.1, 69.4, 69.5, 69.51, 69.52, 69.6, 320.1, 355; 536/23.4, 23.5, 24.1 [IMAGE AVAILABLE]

US PAT NO: 4,889,802 [IMAGE AVAILABLE] L8: 284 of 292

ABSTRACT:
A mammalian myeloma cell comprising a double-stranded DNA molecule in its
genome containing a coding sequence encoding a non-immunoglobulin protein, a non-immunoglobulin promoter sequence adjacent to the 5' terminus of said coding sequence, and the 8-base pair nucleotide sequence
5'-ATTTGCAT-3' located 5' to the transcription initiation site of said promoter sequence. The DNA molecule may optionally contain an enhancer
element. Methods of producing non-immunoglobulin protein and DNA
molecules are also provided.

285. 4,834,976, May 30, 1989, Monoclonal antibodies to pseudomonas
aeruginosa flagella; Mae J. Rosok, et al., 424/142.1, 150.1; 435/7.3, 340, 804, 875; 436/512, 513, 519, 548, 811; 530/388.15, 388.4 [IMAGE
AVAILABLE]

US PAT NO: 4,834,976 [IMAGE AVAILABLE] L8: 285 of 292

ABSTRACT:
Cell lines have been produced that secrete monoclonal antibodies capable
of binding to the flagellar proteins of selected Pseudomonas aeruginosa
strains. Some of these antibodies have been found to be protective against lethal challenges of P. aeruginosa. Pharmaceutical compositions
containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents,
and the prophylactic and therapeutic use of such compositions in the management of infections, are included.
Prior to filing this application, the continuous transformed cell lines PaF4 1VE8, FA6 IIG5, 20H11, and 21B8, described herein, were deposited in
the America Type Culture Collection and given the designations HB9129,
HB9130, CRL 9300, and CRL 9301, respectively.

286. 4,806,312, Feb. 21, 1989, Multizone analytical element having detectable signal concentrating zone; Alfred C. Greenquist, 422/56, 57, 58; 435/7.7, 7.72, 7.92, 805, 968; 436/807, 810, 815 [IMAGE AVAILABLE]

US PAT NO: 4,806,312 [IMAGE AVAILABLE] L8: 286 of 292

ABSTRACT:
A multizone test device for the determination of analyte from a liquid test medium upon contact with the liquid test medium and a labeled reagent comprising a chemical group having a detectable chemical property. The test device preferably comprises multilayers including a reagent layer incorporated with an immobilized reagent and a detection layer incorporated with an immobilized form of an interactive detection
reagent for the labeled reagent. The immobilized reagent in the reagent layer and the labeled reagent comprise specific binding partners which will bind to each other dependent upon the amount of analyte present. Labeled reagent which does not become bound to the immobilized reagent in
the reagent layer migrates into the detection layer and interacts with the immobilized interactive detection reagent therein which results in the localized generation of a detectable reaction product which preferably is also immobilized in the detection zone. As a result, reverse migration of the labeled reagent, and preferably the detectable reaction product from the detection layer is prevented and the detectable
chemical property provided by the label of the labeled reagent is localized in the detection layer for the precise measurement thereof and
correlation to the amount of analyte in the test medium.

287. 4,806,311, Feb. 21, 1989, Multizone analytical element having labeled reagent concentration zone; Alfred C. Greenquist, 422/56, 57, 58;
435/7.4, 7.5, 7.8, 805, 968; 436/807, 810, 815 [IMAGE AVAILABLE]

US PAT NO: 4,806,311 [IMAGE AVAILABLE] L8: 287 of 292

ABSTRACT:
A multizone test device for the determination of analyte from a liquid test medium upon contact with the liquid test medium and a labeled reagent comprising a chemical group having a detectable physical property. The test device preferably comprises multilayers including a reagent layer incorporated with an immobilized reagent and a detection layer incorporated with an immobilized form of a binding substance for
the labeled reagent. The immobilized reagent and the labeled reagent comprise specific binding partners which will bind to each other dependent upon the amount of analyte present. Labeled reagent which does
not become bound to the immobilized reagent in the reagent layer migrates
into the detection layer and becomes bound to and immobilized by the immobilized binding substance therein. As a result, reverse migration of
the labeled reagent into the reagent layer is prevented and the detectable physical property provided by the label of the labeled reagent
is localized in the detection layer for the precise measurement thereof and correlation to the amount of analyte in the test medium.

288. 4,803,156, Feb. 7, 1989, Peptide-beta-lactamase conjugates for enzyme-linked immunoassays; Alexander R. Neurath, et al., 435/5, 7.92,
18, 19; 436/820, 828; 930/142, 200, 221, 222, 223, 260, 310, DIG.820 [IMAGE AVAILABLE]

US PAT NO: 4,803,156 [IMAGE AVAILABLE] L8: 288 of 292

ABSTRACT:
A reagent for an ELISA determination of an antibody, the reagent comprising a peptide covalently linked to beta-lactamase. The reagent can
be used in the following method to detect antibodies in a sample

which
involves
a. contacting the sample with protein A linked to a solid support,
b. incubating the sample-protein A linked to the solid support,
c. washing the incubated sample-protein A linked to the solid support,
d. contacting the washed sample-protein A with the reagent,
e. incubating the sample-protein A and reagent,
f. washing the incubated sample-protein A-reagent, and
g. determining the enzymatic activity of the resultant mass.

289. 4,631,191, Dec. 23, 1986, Methods and compositions useful in preventing equine influenza; Beverly Dale, et al., 424/186.1, 209.1; 530/324, 325, 326, 806, 811; 536/23.72; 930/220, 240 [IMAGE AVAILABLE]

US PAT NO: 4,631,191 [IMAGE AVAILABLE] L8: 289 of 292

ABSTRACT:
Recombinant vaccines for immunizing horses against equine influenza virus
(EIV) are disclosed. The DNA sequences encoding the hemagluttinin (HA)
and neuraminidase (NA) glycoproteins from the two strains of EIV currently infective in horses are used to construct vaccinia carried vaccines, to design synthetic peptides for primer and booster administration, and to permit recombinant synthesis of HA and/or NA protein based vaccines. These DNA sequences also provide probes useful
for preparing similar vaccines from fresh isolates of new strains generated by genetic drift.

290. 4,625,015, Nov. 25, 1986, Broad spectrum influenza antisera; Nicola
Green, et al., 530/324; 424/139.1, 159.1, 186.1, 210.1; 530/328, 387.9, 388.3, 389.4, 403; 930/220, DIG.801, DIG.820 [IMAGE AVAILABLE]

US PAT NO: 4,625,015 [IMAGE AVAILABLE] L8: 290 of 292

ABSTRACT:
Antisera against synthetic peptides which neutralize influenza viruses of
differing hemagglutinin subtypes, provide protection against infection by
influenza virus and methods of preparing the same are disclosed.

291. 4,489,710, Dec. 25, 1984, Composition and method for transplantation therapy; Lynn E. Spitler, 128/898; 424/140.1, 154.1, 183.1, 809; 530/388.75, 391.7, 866 [IMAGE AVAILABLE]

US PAT NO: 4,489,710 [IMAGE AVAILABLE] L8: 291 of 292

ABSTRACT:
An improved transplantion therapy and method is provided which comprises
specifically killing cells known to be problematic in the transplantion process. Novel compositions of the present invention are conjugates prepared by generating antibodies specific to surface receptors of the unwanted cells, preparing Fab or F(ab').sub.2 fragments from the antibodies, and coupling the fragments to A chains of lectins or other cytotoxic agents to render the conjugates thus formed strongly cytotoxic
to the cells to which the antibody was directed. The conjugates are used
in vitro to eliminate unwanted cells prior to bone marrow transplantation.

292. 4,410,634, Oct. 18, 1983, Method of passively adsorbing immuno-reactive haptens to solid phases; Harold R. Cooper, et al., 436/500; 435/7.93, 961, 966; 436/532, 543, 804, 815, 823 [IMAGE AVAILABLE]

US PAT NO: 4,410,634 [IMAGE AVAILABLE] L8: 292 of 292

ABSTRACT:
The method comprises covalently binding an immuno-reactive to a selected
macromolecular carrier and then contacting the resulting hapten-carrier conjugate at a selected concentration in a liquid phase with a selected solid phase until a desired amount of the hapten-carrier conjugate is adsorbed to the surface of the solid phase. Unbound hapten-carrier conjugate is then separated from the solid phase, and the solid phase containing the bound hapten-carrier conjugate is recovered for use in quantitative immunoassays and the like. The solid phase can be, for example, surfaces of a test tube or microtiter well or the like. The method is simple and inexpensive and permits hapten assays of improved
sensitivity.

=> s l8(p)(vector# or construct# or plasmid#)

77317 VECTOR#
96404 CONSTRUCT#
16546 PLASMID#
L9 40 L8(P)(VECTOR# OR CONSTRUCT# OR PLASMID#)

=> d 1- cit ab

1. 5,919,650, Jul. 6, 1999, Method for inactivation of protein function; Mariano Barbacid, et al., 435/69.1, 320.1, 330 [IMAGE AVAILABLE]

US PAT NO: 5,919,650 [IMAGE AVAILABLE] L9: 1 of 40

ABSTRACT:
Method for inactivating the function produced by a protein using an intracellularly expressed antibody or fragment thereof.

2. 5,912,133, Jun. 15, 1999, Method for isolating stem cells expressing
flk-1 receptors; Ihor R. Lemischka, 435/7.21, 971; 530/388.7, 389.6 [IMAGE AVAILABLE]

US PAT NO: 5,912,133 [IMAGE AVAILABLE] L9: 2 of 40

ABSTRACT:
Isolated mammalian nucleic acid molecules encoding receptor protein tyrosine kinases expressed in primitive hematopoietic cells and not expressed in mature hematopoietic cells are provided. Also included are
the receptors encoded by such nucleic acid molecules; the nucleic acid molecules encoding receptor protein tyrosine kinases having the sequences
shown in FIG. 1a (murine flk-2), FIG. 1b (human flk-2) and FIG. 2 (murine
flk-1); the receptor protein tyrosine kinases having the amino acid sequences shown in FIG. 1a, FIG. 1b and FIG. 2; ligands for the receptors; nucleic acid sequences that encode the ligands; and methods of
stimulating the proliferation and/or differentiation of primitive mammalian hematopoietic stem cells comprising contacting the stem cells
with a ligand that binds to a receptor protein tyrosine kinase expressed in primitive mammalian hematopoietic cells and not expressed in mature
hematopoietic cells.

3. 5,885,573, Mar. 23, 1999, Methods and materials for modulation of the
immunosuppressive activity and toxicity of monoclonal antibodies; Jeffrey
A. Bluestone, et al., 424/133.1, 144.1; 530/387.3 [IMAGE AVAILABLE]

US PAT NO: 5,885,573 [IMAGE AVAILABLE] L9: 3 of 40

ABSTRACT:
The binding specificity of the murine OKT3 has been transferred into a
human antibody framework in order to reduce its immunogenicity. This
"humanized" anti-CD3 mAb (gOKT3-5) was previously shown to retain, in
vitro, all the properties of native OKT3, including T cell activation which has been correlated, in vivo, with the severe side-effects observed
in transplant recipients after the first administration of the mAb. Disclosed is a single amino acid mutation from a leucine to a glutamic acid at position 235 in the Fc receptor (FcR) binding segment of the gOKT3-5 mAb to produce Glu-235 mAb. Also disclosed is an amino acid
mutation from the contiguous phenylalanine at position 234 to a

leucine
(Leu-234).

4. 5,877,397, Mar. 2, 1999, Transgenic non-human animals capable of producing heterologous antibodies of various isotypes; Nils Lonberg, et
al., 800/18; 536/23.1, 23.5, 23.53; 800/6 [IMAGE AVAILABLE]

US PAT NO: 5,877,397 [IMAGE AVAILABLE] L9: 4 of 40

ABSTRACT:
The invention relates to transgenic non-human animals capable of producing heterologous antibodies and transgenic non-human animals having
inactivated endogenous immunoglobulin genes. In one aspect of the invention, endogenous immunoglobulin genes are suppressed by antisense
polynucleotides and/or by antiserum directed against endogenous immunoglobulins. Heterologous antibodies are encoded by immunoglobulin
genes not normally found in the genome of that species of non-human animal. In one aspect of the invention, one or more transgenes containing
sequences of unrearranged heterologous human immunoglobulin heavy chains
are introduced into a non-human animal thereby forming a transgenic animal capable of **functionally** rearranging transgenic
immunoglobulin **sequences** and producing a repertoire of **antibodies** of various isotypes encoded by human immunoglobulin genes.
Such heterologous human antibodies are produced in B-cells which are thereafter immortalized, e.g., by fusing with an immortalizing cell line
such as a myeloma or by manipulating such B-cells by other techniques to
perpetuate a cell line capable of producing a monoclonal heterologous antibody. The invention also relates to heavy and light chain
immunoglobulin transgenes for making such transgenic non-human animals as
well as methods and **vectors** for disrupting endogenous immunoglobulin
loci in the transgenic animal.

5. 5,874,264, Feb. 23, 1999, Gibbon ape leukemia virus receptor; Bryan
Mark O'Hara, 435/6, 69.1, 320.1; 530/350; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,874,264 [IMAGE AVAILABLE] L9: 5 of 40

ABSTRACT:
The present invention relates to novel purified gibbon ape leukemia receptor proteins and purified DNA sequences encoding these receptor proteins.

6. 5,871,974, Feb. 16, 1999, Surface expression libraries of heteromeric
receptors; William D. Huse, 435/69.7, 69.1, 252.3, 320.1; 536/23.4 [IMAGE
AVAILABLE]

US PAT NO: 5,871,974 [IMAGE AVAILABLE] L9: 6 of 40

ABSTRACT:
A composition of matter comprising a plurality of procaryotic cells containing diverse combinations of first and second DNA sequences
encoding first and second polypeptides which form a heteromeric receptor
exhibiting binding activity toward a preselected molecule, those heteromeric receptors being expressed on the surface of filamentous bacteriophage.

7. 5,859,309, Jan. 12, 1999, Vector for integration site independent gene expression in mammalian host cells; Sarah Jane Eccles, et al., 800/13; 435/6, 69.1, 91.1, 320.1, 325, 326, 355, 372, 375; 536/24.1; 800/4, 6, 18 [IMAGE AVAILABLE]

US PAT NO: 5,859,309 [IMAGE AVAILABLE] L9: 7 of 40

ABSTRACT:
A **vector** for the integration of a gene into the genetic material of a
mammalian host cell such that the gene may be expressed by the host cell.
The **vector** comprises a promoter and the gene and an immunoglobulin
dominant control region derived from the mouse .lambda. immunoglobulin
gene locus capable of eliciting host cell-type restricted, integration site independent, copy number dependent expression of the said gene. The
DNaseI super hypersensitive site exemplified are i) about 2.35 kb upstream of the CAP site of the rearranged .lambda..sub.1 gene, ii) about
2.5 kb upstream of the genomic V.lambda..sub.2 segment or iii) about 30
kb downstream of the rearranged .lambda..sub.1 gene. Mammalian host cells
transformed with the **vector** are disclosed as are transgenic mammals
transformed with the **vector** and a method of producing a polypeptide
comprising culturing a transformed mammalian cell. A method of gene therapy comprising the steps of i) removing stem cells from the body of a
mammal, ii) optionally killing stem cells remaining in the body, iii) transforming the removed stem cells with the containing a gene deficient
or absent in the body, and iv) replacing the transformed stem cells in the body is also disclosed. Also disclosed is **functional** mouse
immunoglobulin .lambda..sub.1 enhancer consisting of a DNA **sequence** comprising all or a **functional** part of the DNA sequence
between the EcoRI site 3.8 kb downstream of the Xho I site in the rearranged mouse .lambda..sub.1 gene and the SnaBI site 10 kb downstream
of this Xho I site. The functional mouse immunoglobulin .lambda..sub.1
enhancer may comprise all or a functional part of i) the 1.3 kb first HindIII to HindII DNA fragment downstream of the EcoRI site 3.8 kb downstream of the Xho I site in the rearranged mouse .lambda..sub.1 gene,
ii) the 3.3 kb HindII to HindII DNA fragment downstream of the EcoRI site
3.8 kb downstream of the Xho I site in the rearranged mouse .lambda..sub.1 gene and spanning the SnaBI site 10 kb downstream of this
Xho I site.

8. 5,855,887, Jan. 5, 1999, Blockade of lymphocyte down-regulation associated with CTLA-4 signaling; James Patrick Allison, et al., 424/144.1, 133.1, 139.1, 143.1; 435/7.24 [IMAGE AVAILABLE]

US PAT NO: 5,855,887 [IMAGE AVAILABLE] L9: 8 of 40

ABSTRACT:
T cell activation in response to antigen is increased by the administration of binding agents that block CTLA-4 signaling. When CTLA-4
signaling is thus blocked, the T cell response to antigen is released from inhibition. Such an enhanced response is useful for the treatment of
tumors, chronic viral infections, and as an adjuvant during immunization.

9. 5,851,525, Dec. 22, 1998, Recombinant IL-5 antagonists useful in treatment of IL-5 mediated disorders; Robert S. Ames, Jr., et al., 424/145.1, 152.1, 158.1, 172.1; 530/387.1, 387.3, 388.23 [IMAGE AVAILABLE]

US PAT NO: 5,851,525 [IMAGE AVAILABLE] L9: 9 of 40

ABSTRACT:
Chimeric, humanized and other IL-5 mAbs, derived from high affinity neutralizing mAbs, pharmaceutical compositions containing same, methods
of treatment and diagnostics are provided.

10. 5,840,540, Nov. 24, 1998, Nucleic acids encoding presenilin II; Peter H. St. George-Hyslop, et al., 435/69.1, 252.3, 320.1, 325; 530/350;
536/23.1, 24.3 [IMAGE AVAILABLE]

US PAT NO: 5,840,540 [IMAGE AVAILABLE] L9: 10 of 40

ABSTRACT:
The present invention describes the identification, isolation and cloning
of two human presenilin genes, PS-1 and PS-2, mutations in which lead to
Familial Alzheimer's Disease. Also identified are presenilin homologue
genes in mice, C. elegans and D. melanogaster. Transcripts and products
of these genes are useful in detecting and diagnosing Alzheimer's disease, developing therapeutics for treatment of Alzheimer's disease, as
well as the isolation and manufacture of the protein and the constructions of transgenic animals expressing the mutant genes.

11. 5,840,300, Nov. 24, 1998, Methods and compositions comprising single
chain recombinant antibodies; William V. Williams, et al., 424/135.1, 148.1; 530/324, 325, 326, 388.35; 536/23.1 [IMAGE AVAILABLE]

US PAT NO: 5,840,300 [IMAGE AVAILABLE] L9: 11 of 40

ABSTRACT:
Methods and compositions for the generation of single chain antibody fragments.

12. 5,817,308, Oct. 6, 1998, Tolerogenic fusion proteins of immunoglobulins and methods for inducing and maintaining tolerance; David
W. Scott, et al., 424/93.21, 130.1, 133.1, 184.1, 185.1; 435/91.31, 320.1, 325, 326, 328; 514/44; 530/387.3; 536/22.1, 23.1 [IMAGE AVAILABLE]

US PAT NO: 5,817,308 [IMAGE AVAILABLE] L9: 12 of 40

ABSTRACT:
The invention provides methods and compositions for inducing and maintaining tolerance to epitopes or antigens containing the epitopes. The compositions include expression cassettes and **vectors** including
DNA **sequences** coding for a fusion **immunoglobulin** operably linked
to transcriptional and translational control regions **functional** in a hemopoietic or lymphoid cell. The fusion immunoglobulin includes at least
one heterologous tolerogenic epitope at the N-terminus variable region of
the immunoglobulin. Cells stably transformed with the expression **vector** are formed and used to produce fusion immunoglobulin. The
invention also provides methods for screening for novel tolerogenic epitopes and for inducing and maintaining tolerance. The methods of the
invention are useful in the diagnosis and treatment of autoimmune or allergic immune responses.

13. 5,814,318, Sep. 29, 1998, Transgenic non-human animals for producing
heterologous antibodies; Nils Lonberg, et al., 424/184.1; 435/69.6; 530/387.1; 536/23.1, 23.53; 800/6 [IMAGE AVAILABLE]

US PAT NO: 5,814,318 [IMAGE AVAILABLE] L9: 13 of 40

ABSTRACT:
The invention relates to transgenic non-human animals capable of producing heterologous antibodies and transgenic non-human animals having
inactivated endogenous immunoglobulin genes. In one aspect of the invention, endogenous immunoglobulin genes are suppressed by antisense
polynucleotides and/or by antiserum directed against endogenous immunoglobulins. Heterologous antibodies are encoded by immunoglobulin
genes not normally found in the genome of that species of non-human animal. In one aspect of the invention, one or more transgenes containing
sequences of unrearranged heterologous human immunoglobulin heavy chains
are introduced into a non-human animal thereby forming a transgenic animal capable of **functionally** rearranging transgenic **immunoglobulin** **sequences** and producing a repertoire of **antibodies** of various isotypes encoded by human immunoglobulin genes.
Such heterologous human antibodies are produced in B-cells which are thereafter immortalized, e.g., by fusing with an immortalizing cell line such as a myeloma or by manipulating such B-cells by other techniques to
perpetuate a cell line capable of producing a monoclonal heterologous antibody. The invention also relates to heavy and light chain immunoglobulin transgenes for making such transgenic non-human animals as
well as methods and **vectors** for disrupting endogenous immunoglobulin
loci in the transgenic animal.

14. 5,811,097, Sep. 22, 1998, Blockade of T lymphocyte down-regulation
associated with CTLA-4 signaling; James Patrick Allison, et al., 424/144.1, 130.1, 133.1, 135.1, 141.1, 143.1, 152.1, 154.1, 810; 514/2, 12, 885; 530/387.1, 387.3, 388.1, 388.22, 388.7 [IMAGE AVAILABLE]

US PAT NO: 5,811,097 [IMAGE AVAILABLE] L9: 14 of 40

ABSTRACT:
T cell activation in response to antigen is increased by the administration of binding agents that block CTLA-4 signaling. When CTLA-4
signaling is thus blocked, the T cell response to antigen is released from inhibition. Such an enhanced response is useful for the treatment of
tumors, chronic viral infections, and as an adjuvant during immunization.

15. 5,789,650, Aug. 4, 1998, Transgenic non-human animals for producing
heterologous antibodies; Nils Lonberg, et al., 800/18; 530/387.1 [IMAGE
AVAILABLE]

US PAT NO: 5,789,650 [IMAGE AVAILABLE] L9: 15 of 40

ABSTRACT:
The invention relates to transgenic non-human animals capable of producing heterologous antibodies and transgenic non-human animals having
inactivated endogenous immunoglobulin genes. In one aspect of the invention, endogenous immunoglobulin genes are suppressed by antisense
polynucleotides and/or by antiserum directed against endogenous immunoglobulins. Heterologous antibodies are encoded by immunoglobulin
genes not normally found in the genome of that species of non-human animal. In one aspect of the invention, one or more transgenes containing
sequences of unrearranged heterologous human immunoglobulin heavy chains
are introduced into a non-human animal thereby forming a transgenic animal capable of **functionally** rearranging transgenic **immunoglobulin** **sequences** and producing a repertoire of **antibodies** of various isotypes encoded by human immunoglobulin genes.
Such heterologous human antibodies are produced in B-cells which are thereafter immortalized, e.g., by fusing with an immortalizing cell line such as a myeloma or by manipulating such B-cells by other techniques to
perpetuate a cell line capable of producing a monoclonal heterologous antibody. The invention also relates to heavy and light chain immunoglobulin transgenes for making such transgenic non-human animals as
well as methods and **vectors** for disrupting endogenous immunoglobulin
loci in the transgenic animal.

16. 5,783,420, Jul. 21, 1998, Method and compositions for controlling gene expression; Eric H. Davidson, 435/69.1, 320.1; 536/23.4, 23.53, 24.1
[IMAGE AVAILABLE]

US PAT NO: 5,783,420 [IMAGE AVAILABLE] L9: 16 of 40

ABSTRACT:
The present invention is directed to methods and compositions useful for
altering the transcriptional expression of genes in eukaryotic cells. The

invention employs novel antibody derivative molecules which **function**
to recognize and bind to specific cis-regulatory DNA **sequence** elements of a eukaryotic gene. When two **antibody** derivative molecules
are bound to adjacent cis-regulatory DNA sequence elements of a gene,
those molecules may interact to form an antibody binding site which is capable of recognizing and binding to a transcription factor protein for the target gene, thereby affecting the functionality of that transcription factor protein and, in turn, the transcriptional activity of the gene. Also provided herein are isolated nucleic acids encoding the
novel antibody derivative molecules of the present invention and expression **vectors** comprising those nucleic acids.

17. 5,783,184, Jul. 21, 1998, Method for treatment and diagnosis of IL-5
mediated disorders; Edward Robert Appelbaum, et al., 424/130.1, 133.1,
141.1, 145.1; 435/7.1; 530/388.1, 388.23 [IMAGE AVAILABLE]

US PAT NO: 5,783,184 [IMAGE AVAILABLE] L9: 17 of 40

ABSTRACT:
The present invention relates to treatment and diagnosis of conditions mediated by IL-5 and excess eosinophil production, and more specifically
to mAbs and other altered antibodies such as Fabs, chimeric, human and
humanized antibodies that do not block binding of human IL-5 to the .alpha.-chain of the human IL-5 receptor.

18. 5,776,677, Jul. 7, 1998, Methods of detecting cystic fibrosis gene by nucleic acid hybridization; Lap-Chee Tsui, et al., 435/6, 91.2; 536/23.2, 24.3, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,776,677 [IMAGE AVAILABLE] L9: 18 of 40

ABSTRACT:
The cystic fibrosis gene and its gene product are described for both the normal and mutant forms. The genetic and protein information is used in
developing DNA diagnosis, protein diagnosis, carrier and patient screening, drug and gene therapy, cloning of the gene and manufacture of
the protein, and development of cystic fibrosis affected animals.

19. 5,770,449, Jun. 23, 1998, Vector for integration site independent gene expression in mammalian host cells which permit immunoglobulin gene
expression; Sarah Jane Eccles, et al., 435/375, 69.1, 70.3, 70.4, 320.1, 455; 514/44 [IMAGE AVAILABLE]

US PAT NO: 5,770,449 [IMAGE AVAILABLE] L9: 19 of

ABSTRACT:
A **vector** for the integration of a gene into the genetic material of a
mammalian host cell such that the gene may be expressed by the host cell.
The **vector** comprises a promoter and the gene and in an immunoglobulin
dominant control region derived from the mouse .lambda. immunoglobulin
gene locus capable of eliciting host cell-type restricted, integration site independent, copy number dependent expression of said gene. The DNaseI super hypersensitive site exemplified are i) about 2.35 kb upstream of the CAP site of the rearranged .lambda..sub.1 gene, ii) about
2.5 kb upstream of the genomic V.lambda..sub.2 segment or iii) about 30
kb downstream of the rearranged .lambda..sub.1 gene. Mammalian host cells
transformed with the **vector** are disclosed as are transgenic mammals
transformed with the **vector** and a method of producing a polypeptide
comprising culturing a transformed mammalian cell. A method of gene therapy comprising the steps of i) removing stem cells from the body of a
mammal, ii) optionally killing stem cells remaining in the body, iii) transforming the removed stem cells with the **vector** containing a gene
deficient or absent in the body, and iv) replacing the transformed stem cells in the body is also disclosed. Also disclosed is **functional** mouse **immunoglobulin** .lambda..sub.1 enhancer consisting of a DNA
sequence comprising all or a **functional** part of the DNA sequence
between the EcoRI site 3.8 kb downstream of the Xho I site in the rearranged mouse .lambda..sub.1 gene and the SnaBI site 10 kb downstream
of this Xho I site. The functional mouse immunoglobulin .lambda..sub.1
enhancer may comprise all or a functional part of i) the 1.3 kb first HindIII to HindIII DNA fragment downstream of the EcoRI site 3.8 kb
downstream of the Xho I site in the rearranged mouse .lambda..sub.1 gene,
ii) the 3.3 kb HindIII to HindIII DNA fragment downstream of the EcoRI
site 3.8 kb downstream of the Xho I site in the rearranged mouse .lambda..sub.1 gene and spanning the SnaBI site 10 kb downstream of this
Xho I site.

20. 5,747,651, May 5, 1998, Antibodies against tyrosine kinase receptor
flk-1; Ihor R. Lemischka, 530/387.9, 388.22, 388.7, 389.1, 389.6 [IMAGE

AVAILABLE]

US PAT NO: 5,747,651 [IMAGE AVAILABLE] L9: 20 of 40

ABSTRACT:
Isolated mammalian nucleic acid molecules encoding receptor protein tyrosine kinases expressed in primitive hematopoietic cells and not expressed in mature hematopoietic cells are provided. Also included are
the receptors encoded by such nucleic acid molecules; the nucleic acid molecules encoding receptor protein tyrosine kinases having the sequences
shown in FIG. 1a (murine flk-2), FIG. 1b (human flk-2) and FIG. 2 (murine
flk-1); the receptor protein tyrosine kinases having the amino acid sequences shown in FIG. 1a, FIG. 1b and FIG. 2; ligands for the receptors; nucleic acid sequences that encode the ligands; and methods of
stimulating the proliferation and/or differentiation of primitive mammalian hematopoietic stem cells comprising contacting the stem cells
with a ligand that binds to a receptor protein tyrosine kinase expressed in primitive mammalian hematopoietic cells and not expressed in mature
hematopoietic cells.

21. 5,712,379, Jan. 27, 1998, Method and compositions for controlling gene expression; Eric H. Davidson, 536/23.4; 435/69.7; 536/23.53 [IMAGE
AVAILABLE]

US PAT NO: 5,712,379 [IMAGE AVAILABLE] L9: 21 of 40

ABSTRACT:
The present invention is directed to methods and compositions useful for
altering the transcriptional expression of genes in eukaryotic cells. The invention employs novel antibody derivative molecules which **function**
to recognize and bind to specific cis-regulatory DNA **sequence** elements of a eukaryotic gene. When two **antibody** derivative molecules
are bound to adjacent cis-regulatory DNA sequence elements of a gene,
those molecules may interact to form an antibody binding site which is capable of recognizing and binding to a transcription factor protein for the target gene, thereby affecting the functionality of that transcription factor protein and, in turn, the transcriptional activity of the gene. Also provided herein are isolated nucleic acids encoding the
novel antibody derivative molecules of the present invention and expression **vectors** comprising those nucleic acids.

22. 5,698,426, Dec. 16, 1997, Surface expression libraries of heteromeric receptors; William D. Huse, 435/91.41, 69.1, 69.7, 320.1,

475; 530/387.1 [IMAGE AVAILABLE]

US PAT NO: 5,698,426 [IMAGE AVAILABLE] L9: 22 of 40

ABSTRACT:
A composition of matter comprising a plurality of procaryotic cells containing diverse combinations of first and second DNA sequences encoding first and second polypeptides which form a heteromeric receptor
exhibiting binding activity toward a preselected molecule, said heteromeric receptors being expressed on the surface of filamentous bacteriophage.

23. 5,693,323, Dec. 2, 1997, Recombinant IL-5 antagonists useful in treatment of IL-5 mediated disorders; Robert S. Ames, Jr., et al., 424/145.1; 435/328, 335; 530/387.3, 388.23 [IMAGE AVAILABLE]

US PAT NO: 5,693,323 [IMAGE AVAILABLE] L9: 23 of 40

ABSTRACT:
Chimeric, humanized and other IL-5 mAbs, derived from high affinity neutralizing mAbs, pharmaceutical compositions containing same, methods
of treatment and diagnostics are provided.

24. 5,683,892, Nov. 4, 1997, DNA encoding recombinant IL-5 antagonists
useful in treatment of IL-5 mediated disorders; Robert S. Ames, Jr., et al., 435/69.1, 69.3, 70.21, 252.3, 320.1, 328; 536/23.53 [IMAGE AVAILABLE]

US PAT NO: 5,683,892 [IMAGE AVAILABLE] L9: 24 of 40

ABSTRACT:
DNA encoding chimeric, humanized and other IL-5 mAbs, derived from high
affinity neutralizing mAbs, pharmaceutical compositions containing same,
methods of treatment and diagnostics are provided.

25. 5,681,942, Oct. 28, 1997, Fanconi Anemia Type C gene; Manuel Buchwald, et al., 536/23.5, 24.2, 24.31, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,681,942 [IMAGE AVAILABLE] L9: 25 of 40

ABSTRACT:
Fanconi Anemia is a human genetic disease, the precise cause of which is,
to date, unknown. This invention provides an isolated human cDNA molecule
which is able to specifically complement, in one type of Fanconi Anemia,
(type C) the characteristic defect exhibited by cells derived from patients with Fanconi Anemia. The genomic gene from which this cDNA is
derived is also provided as is the sequence of the protein encoded by this gene. Mutations in this gene are proposed to underlie Fanconi Anemia
Type C. Diagnostic and therapeutic applications which derive from this
work are described. The murine homolog of the human cDNA is also provided.

26. 5,661,016, Aug. 26, 1997, Transgenic non-human animals capable of
producing heterologous antibodies of various isotypes; Nils Lonberg, et
al., 435/452; 424/184.1; 435/91.1; 530/387.1; 536/23.1, 23.53 [IMAGE
AVAILABLE]

US PAT NO: 5,661,016 [IMAGE AVAILABLE] L9: 26 of 40

ABSTRACT:
The invention relates to transgenic non-human animals capable of producing heterologous antibodies and transgenic non-human animals having
inactivated endogenous immunoglobulin genes. In one aspect of the invention, endogenous immunoglobulin genes are suppressed by antisense
polynucleotides and/or by antiserum directed against endogenous immunoglobulins. Heterologous antibodies are encoded by immunoglobulin
genes not normally found in the genome of that species of non-human animal. In one aspect of the invention, one or more transgenes containing
sequences of unrearranged heterologous human immunoglobulin heavy chains
are introduced into a non-human animal thereby forming a transgenic animal capable of **functionally** rearranging transgenic **immunoglobulin** **sequences** and producing a repertoire of **antibodies** of various isotypes encoded by human immunoglobulin genes.
Such heterologous human antibodies are produced in B-cells which are thereafter immortalized, e.g., by fusing with an immortalizing cell line such as a myeloma or by manipulating such B-cells by other techniques to
perpetuate a cell line capable of producing a monoclonal heterologous antibody. The invention also relates to heavy and light chain immunoglobulin transgenes for making such transgenic non-human animals as
well as methods and **vectors** for disrupting endogenous immunoglobulin
loci in the transgenic animal.

27. 5,627,052, May 6, 1997, Methods for the production of proteins with
a desired function; John W. Schrader, 435/69.6, 465; 530/387.1, 388.24
[IMAGE AVAILABLE]

US PAT NO: 5,627,052 [IMAGE AVAILABLE] L9: 27 of 40

ABSTRACT:
The present invention provides a method for producing proteins with a desired function, generally comprising the steps of (a) providing a population of antibody-forming cells suspected of containing at least one
cell capable of producing an antibody exhibiting a desired function; (b) suspending the population of antibody-forming cells in a medium, the medium having an indicator system incorporated therein, the indicator system also being capable of indicating the presence and location of a cell which forms antibodies exhibiting the desired function; (c) identifying a cell forming an antibody exhibiting the desired function; (d) isolating the identified antibody-forming cell from the medium; (e) determining the amino acid sequence of the variable region or a portion
thereof which coffers the desired function of the antibody produced by the isolated antibody-forming cell; and (f) synthesizing a protein with a desired function, the protein containing the amino acid sequence of the variable region or portion thereof which confers the desired function.

28. 5,601,988, Feb. 11, 1997, Immunocapture assay for cancer procoagulant antibody complex in biological samples; Stuart G. Gordon,
435/7.23, 7.92, 7.94, 975; 436/63, 64, 507, 813 [IMAGE AVAILABLE]

US PAT NO: 5,601,988 [IMAGE AVAILABLE] L9: 28 of 40

ABSTRACT:
This invention provides a specific immunocapture ELISA for the quantitation of cancer procoagulant antibody complex (CPAC) in biological
samples. In particular, this invention provides methods and techniques for specifically selecting and quantitatively measuring CPAC from a sample material using anti-CP antibodies followed by labeled anti-immunoglobulin antibodies. The amount of captured CPAC is then
determined by measuring the amount of label in the captured CPAC.

29. 5,556,744, Sep. 17, 1996, Methods and compositions for diagnosing
and treating certain HIV infected patients; David B. Weiner, et al., 435/5, 7.1, 974, 975; 530/324, 325, 326, 327, 328, 826 [IMAGE AVAILABLE]

US PAT NO: 5,556,744 [IMAGE AVAILABLE] L9: 29 of 40

ABSTRACT:
The present invention provides a panel of HIV peptides useful in diagnosing whether or not a patient is of vertical HIV transmission

status, methods for diagnosing same, methods for identifying epitopes and
peptides associated with non-transmission status, and pharmaceutical and
vaccine compositions containing same.

30. 5,548,065, Aug. 20, 1996, Tyrosine kinase receptor human flk-2-specific antibodies; Ihor R. Lemischka, 530/388.22, 387.9, 388.23,
388.7, 389.2, 389.6 [IMAGE AVAILABLE]

US PAT NO: 5,548,065 [IMAGE AVAILABLE] L9: 30 of 40

ABSTRACT:
Isolated mammalian nucleic acid molecules encoding receptor protein tyrosine kinases expressed in primitive hematopoietic cells and not expressed in mature hematopoietic cells are provided. Also included are
the receptors encoded by such nucleic acid molecules; the nucleic acid molecules encoding receptor protein tyrosine kinases having the sequences
shown in FIG. 1a (murine flk-2), FIG. 1b (human flk-2) and FIG. 2 (murine
flk-1); the receptor protein tyrosine kinases having the amino acid sequences shown in FIG. 1a, FIG. 1b and FIG. 2; ligands for the receptors; nucleic acid sequences that encode the ligands; and methods of
stimulating the proliferation and/or differentiation of primitive mammalian hematopoietic stem cells comprising contacting the stem cells
with a ligand that binds to a receptor protein tyrosine kinase expressed in primitive mammalian hematopoietic cells and not expressed in mature
hematopoietic cells.

31. 5,545,806, Aug. 13, 1996, Ransgenic non-human animals for producing
heterologous antibodies; Nils Lonberg, et al., 800/6; 424/184.1; 435/69.6, 320.1; 536/23.1, 23.5, 23.53; 800/18 [IMAGE AVAILABLE]

US PAT NO: 5,545,806 [IMAGE AVAILABLE] L9: 31 of 40

ABSTRACT:
The invention relates to transgenic non-human animals capable of producing heterologous antibodies and transgenic non-human animals having
inactivated endogenous immunoglobulin genes. In one aspect of the invention, endogenous immunoglobulin genes are suppressed by antisense
polynucleotides and/or by antiserum directed against endogenous immunoglobulins. Heterologous antibodies are encoded by immunoglobulin
genes not normally found in the genome of that species of non-human animal. In one aspect of the invention, one or more transgenes containing
sequences of unrearranged heterologous human immunoglobulin heavy chains
are introduced into a non-human animal thereby forming a transgenic animal capable of **functionally** rearranging transgenic **immunoglobulin** **sequences** and producing a repertoire of **antibodies** of various isotypes encoded by human immunoglobulin genes.
Such heterologous human antibodies are produced in B-cells which are thereafter immortalized, e.g., by fusing with an immortalizing cell line such as a myeloma or by manipulating such B-cells by other techniques to
perpetuate a cell line capable of producing a monoclonal heterologous antibody. The invention also relates to heavy and light chain immunoglobulin transgenes for making such transgenic non-human animals as
well as methods and **vectors** for disrupting endogenous immunoglobulin
loci in the transgenic animal.

32. 5,429,746, Jul. 4, 1995, Antibody purification; Paula J. Shadle, et al., 210/635, 656; 530/390.5, 413, 417 [IMAGE AVAILABLE]

US PAT NO: 5,429,746 [IMAGE AVAILABLE] L9: 32 of 40

ABSTRACT:
This invention relates to the application of hydrophobic interaction chromatography combination chromatography to the purification of antibody
molecule proteins.

33. 5,424,398, Jun. 13, 1995, Peptides and nucleic acid sequences related to the Epstein Barr virus; Jaap M. Middeldorp, et al., 530/350, 387.1 [IMAGE AVAILABLE]

US PAT NO: 5,424,398 [IMAGE AVAILABLE] L9: 33 of 40

ABSTRACT:
The present invention relates to peptides immunochemically reactive with
antibodies to the Epstein-Barr virus (EBV), comprising at least part of the VCA-p18 or VCA-p40 protein, encoded within the EBV open reading
frames BFRF3 and BdRF1 respectively, or a **functional** variant thereof.
The invention further relates to nucleic acid **sequences** encoding these peptides, monoclonal **antibodies** against these peptides, cell lines capable of producing monoclonal antibodies and anti-idiotype antibodies. The invention also relates to recombinant **vector** molecules comprising a nucleic acid sequence according to the invention
and host cells transformed or transfected with these **vector** molecules. The invention is further concerned with immunological reagents
and methods for the detection of EBV or anti-EBV antibodies and a method
for the amplification and detection of Epstein Barr viral nucleic acid.

34. 5,414,076, May 9, 1995, DNA encoding gibbon ape leukemia virus
receptor; Bryan M. O'Hara, 536/23.5; 530/324, 325, 326, 327, 328, 329,
350 [IMAGE AVAILABLE]

US PAT NO: 5,414,076 [IMAGE AVAILABLE] L9: 34 of 40

ABSTRACT:
The present invention relates to the gibbon ape leukemia virus (GALV)
receptor protein and gene, as well as methods for regulating viral entry into cells.

35. 5,413,907, May 9, 1995, Diagnosis for malignant hyperthermia; Ronald
G. Worton, et al., 435/6; 536/23.5, 24.31 [IMAGE AVAILABLE]

US PAT NO: 5,413,907 [IMAGE AVAILABLE] L9: 35 of 40

ABSTRACT:

A method for isolating a cDNA specific for the human ryanodine receptor
is disclosed. The gene is associated with malignant hyperthermia, a hypermetabolic syndrome triggered primarily by inhalation anesthetics. The cDNA can be cloned and expressed in a recombinant plasmid or phage.
The cDNA, or fragments thereof, is used as diagnostic probes for individuals at risk for malignant hyperthermia using restriction fragment
length polymorphism analysis. The cDNA is that sequenced in FIG. 2 of
this specification.

36. 5,367,057, Nov. 22, 1994, Tyrosine kinase receptor flk-2 and fragments thereof; Ihor R. Lemischka, 530/350, 403 [IMAGE AVAILABLE]

US PAT NO: 5,367,057 [IMAGE AVAILABLE] L9: 36 of 40

ABSTRACT:
Isolated mammalian nucleic acid molecules encoding receptor protein tyrosine kinases expressed in primitive hematopoietic cells and not expressed in mature hematopoietic cells are provided. Also included are
the receptors encoded by such nucleic acid molecules; the nucleic acid molecules encoding receptor protein tyrosine kinases having the sequences
shown in FIG. 1 (murine flk-2), FIG. 2 (human flk-2) and FIG. 3 (murine

flk-1); the receptor protein tyrosine kinases having the amino acid sequences shown in FIG. 1 (murine flk-2); FIG. 2 (human flk-2) and FIG.
3; ligands for the receptors; nucleic acid sequences that encode the ligands; and methods of stimulating the proliferation and/or differentiation of primitive mammalian hematopoietic stem cells comprising contacting the stem cells with a ligand that binds to a receptor protein tyrosine kinase expressed in primitive mammalian hematopoietic cells and not expressed in mature hematopoietic cells.

37. 5,358,649, Oct. 25, 1994, Diagnosis for porcine malignant hyperthermia; David H. MacLennan, et al., 435/6, 91.2; 536/24.31, 24.33
[IMAGE AVAILABLE]

US PAT NO: 5,358,649 [IMAGE AVAILABLE] L9: 37 of 40

ABSTRACT:

A purified DNA molecule comprises a DNA sequence of approximately 15.1
kb coding for normal or mutant RYR1 protein having a molecular weight of
approximately 564,740 daltons. The DNA molecule has an endonuclease
restriction map of FIG. 1 and a sequence of FIG. 2.

38. 5,270,458, Dec. 14, 1993, Nucleic acids encoding fragments of hematopoietic stem cell receptor flk-2; Ihor R. Lemischka, 536/23.5; 435/69.1, 320.1; 530/350, 403 [IMAGE AVAILABLE]

US PAT NO: 5,270,458 [IMAGE AVAILABLE] L9: 38 of 40

ABSTRACT:
Isolated mammalian nucleic acid molecules encoding receptor protein tyrosine kinases expressed in primitive hematopoietic cells and not expressed in mature hematopoietic cells are provided. Also included are
the receptors encoded by such nucleic acid molecules; the nucleic acid molecules encoding receptor protein tyrosine kinases having the sequences
shown in FIG. 1a (murine flk-2), FIG. 1b (human flk-2) and FIG. 2 (murine
flk-1); the receptor protein tyrosine kinases having the amino acid sequences shown in FIG. 1a, FIG. 1b and FIG. 2; ligands for the receptors; nucleic acid sequences that encode the ligands; and methods of
stimulating the proliferation and/or differentiation of primitive mammalian hematopoietic stem cells comprising contacting the stem cells
with a ligand that binds to a receptor protein tyrosine kinase expressed in primitive mammalian hematopoietic cells and not expressed in mature
hematopoietic cells.

39. 5,151,361, Sep. 29, 1992, Host cells expressing gibbon ape leukemia
virus receptor; Bryan M. O'Hara, 435/354, 69.1, 254.2; 530/350 [IMAGE
AVAILABLE]

US PAT NO: 5,151,361 [IMAGE AVAILABLE] L9: 39 of 40

ABSTRACT:
The present invention relates to novel purified gibbon ape leukemia receptor proteins and purified DNA sequences encoding these receptor proteins. The invention also relates to a method for identifying receptor
proteins using the isolated DNA sequence as a probe, and a method for regulating viral entry into cells by manipulation of the GALV receptor.

40. 4,975,369, Dec. 4, 1990, Recombinant and chimeric KS1/4 antibodies
directed against a human adenocarcinoma antigen; Lisa S. Beavers, et al.,
435/69.1, 320.1, 464, 465; 530/387.3, 388.15, 388.85, 867; 536/23.53, 23.72 [IMAGE AVAILABLE]

US PAT NO: 4,975,369 [IMAGE AVAILABLE] L9: 40 of 40

ABSTRACT:
The present invention comprises novel recombinant DNA compounds which
encode monoclonal antibody KS1/4 and chimeric derivatives of monoclonal
antibody KS1/4. Eukaryotic expression vectors have been constructed that
comprise novel KS1/4-encoding DNA and drive expression of KS1/4 when
transformed into an appropriate host cell. The novel expression vectors can be used to create modified and chimeric derivatives of KS1/4. The recombinant-produced KS1/4, KS1/4 derivatives and KS1/4 chimeras are
useful for the diagnosis, prognosis and treatment of disease states including adenocarcinoma.

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